AUG 2 0 1945

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THE JOURNAL

OF THE

American Medical Association

Subscription, $8.00 | Published Weekly at | *Single Copy, 25 Cents*

VOLUME 128, No. 16 | 535 North Dearborn Street, Chicago 10, Illinois | AUGUST 18, 1945

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association. Subscription price, $8.00 a year. 25c a copy. Canadian $9.50. Foreign $12.00. Entered as second class matter June 25, 1885 at the Postoffice at Chicago, Ill., under act of March 3, 1879. Address all communications to American Medical Association, 535 N. Dearborn St., Chicago 10, Illinois.

The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 128, No. 16 CHICAGO, ILLINOIS AUGUST 18, 1945

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HUMAN ENCEPHALITIS IN THE YAKIMA VALLEY, WASHINGTON, 1942

WITH FORTY-NINE VIRUS ISOLATIONS (WESTERN EQUINE AND ST. LOUIS TYPES) FROM MOSQUITOES

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SAN FRANCISCO

In the Yakima Valley, Washington, a series of four annual epidemics of encephalitis have occurred. The present report is concerned with the last of these outbreaks (1942), which is the third studied and reported. The findings of this investigation warrant reporting, particularly since the cases were followed more carefully clinically, since a higher proportion of both early and late phase serums were obtained for neutralization tests, and especially since 49 virus isolations were made from mosquitoes caught in the epidemic area. Identification of these viruses and repeated titrations of antibody in the patients' serums have greatly delayed this report, but during the interval certain other significant data have been collected and experiments performed which contribute greatly to the analysis of the problem. Furthermore, it may now be recorded that two succeeding summers (1943-1944) have passed during which there has been no encephalitis epidemic in the valley. Only 1 human case was recognized in 1943. This terminated fatally and we succeeded in obtaining from the brain the first strain of western equine virus to be isolated directly from man from this area. Studies are in progress to attempt to discover what may have brought about this break in the series of epidemics.

During the late summer of 1942, 28 cases of encephalitis were sufficiently well diagnosed to be included in this series. These include cases of the western equine and St. Louis types and probably at least one other whose etiologic agent has not been identified. We [1] reported 31 cases in 1939, 58 in 1940 and 26 in 1941. Chart 1 shows the seasonal distribution of cases for the four years. From the standpoint of temperature, humidity and mosquito prevalence the summer of 1942 did not vary significantly from the two previous years; the temperature rose to 90 F. or above almost every day, there was no measurable precipitation, and mosquitoes bred abundantly in many places, principally as a result of careless irrigation practices.

We were assisted during part of the entomologic survey by Mr. Theodore Aarons and in the laboratory work by Mrs. Anne Thorpe, technician.

From the George Williams Hooper Foundation for Medical Research, University of California, San Francisco, and the Yakima City-County Health Department, Yakima, Wash.

This investigation was carried out under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of California and in cooperation with the Washington State Health Department and the U. S. Department of Agriculture, Bureau of Entomology and Plant Quarantine, Division of Insects Affecting Man and Animals. Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

CLINICAL OBSERVATIONS

Diagnosis in all but 1 case was confirmed by some laboratory procedure. In most instances the spinal fluid was examined in the clinical laboratory, and in the virus laboratory serum antibody titrations were made to both western equine and St. Louis viruses. In a number of instances tests were made for antibodies to Japanese B encephalitis virus, the latter all with negative results (table 1). In 5 instances in which cases were seen very soon after the onset, throat and nasal washings, after centrifugation at 18,000 revolutions per minute, were tested for the presence of a virus by intracerebral mouse inoculation. These tests were also negative. One of us (W. M. H.) saw practically every patient in consultation, and most of the patients were visited daily or at frequent intervals throughout the period of illness.

In table 1 are presented the results of the serum neutralization tests. It will be noted at a glance that, although this probably represents the most complete series of early and convalescent phase serums yet reported, in but a few instances have the tests made it possible to make an etiologic diagnosis. It certainly indicates that a test on a single convalescent specimen is without value, unless negative.

In each instance the convalescent serum was first tested to determine the presence or absence of antibodies. If positive it was then simultaneously titrated in serial threefold or fivefold dilutions against a dilution of virus representing approximately ten to fifteen LD_{50} intracerebral mouse doses. Most positive serums showed some protection to this amount of either virus in a dilution of 1:125 or 1:625 and occasionally higher. It was found that results obtained when employing the more common method of titrating undiluted serum against serial dilutions of virus were very unreliable in that if repeated at a later date great discrepancies were occasionally noted. Because the factors involved were not understood at the time and therefore could

1. Hammon, W. M.: Encephalitis in the Yakima Valley: Mixed St. Louis and Western Equine Types, J. A. M. A. **117**: 161-167 (July 19) 1941. Hammon, W. M., and Howitt, Beatrice F.: Epidemiological Aspects of Encephalitis in the Yakima Valley, Washington: Mixed St. Louis and Western Equine Types, Am. J. Hyg. **35**: 163-186 (March) 1942. Hammon, W. M.: Encephalitis: Eastern and Western Equine and St. Louis Types, as Observed in 1941 in Washington, Arizona, New Mexico and Texas, J. A. M. A. **121**: 560-564 (Feb. 20) 1943.

not be controlled, the more satisfactory method of serum dilution was substituted. Many minor modifications of the method were tried, and most serums were tested repeatedly.

In 6 instances the titer of antibodies to the western equine virus showed a definite increase. In 2 other cases serologic evidence of an almost incontrovertible nature led to a similar diagnosis of this type infection. These were 2 infants aged 5 and 8 weeks who had antibodies to western equine virus in the one serum specimen obtained, and in neither instance was any antibody present at the same time in the mother's serum.

St. Louis virus antibodies were present in the serums of these same 2 infants and their mothers, but when comparative titrations were made the titer of each infant's serum was much below that of the respective mother. This represents in all probability placentally transmitted St. Louis virus antibody in the infants' serums with titers well below those of the mothers at a period of five to eight weeks after birth.

Five patients developed an increase in antibody titer to the St. Louis virus, but 2 of these also showed an increase in titer for the western equine strain. This

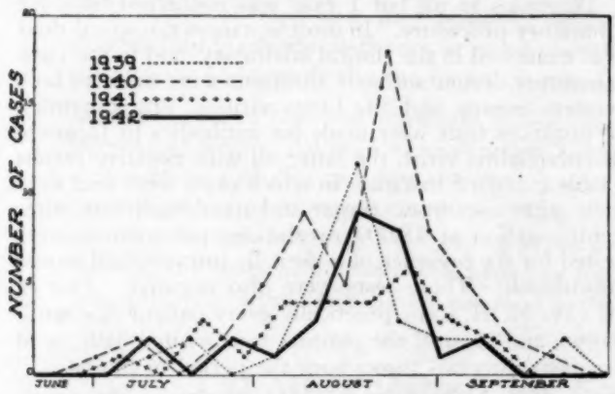

Chart 1.—Cases of encephalitis by weeks, 1939-1942.

increase to both viruses has been reported by us previously and suggestions were made regarding interpretation.[2]

The serums of 10 patients from whom early and late specimens were obtained failed to show an increase of titer to either virus, yet the clinical manifestations, including the spinal fluid findings, were of a nature similar to the others in which the serologic findings were positive (case 13). One of the 10 had antibody to the western equine virus alone, with no change in titer. Six had both western equine and St. Louis antibodies, but the titer of both remained constant. Two had antibodies to St. Louis virus alone, both without change. One had no antibodies to either virus. The last group to be considered includes those from whom only one or no specimen of blood was obtained, or whose serum titration for one virus showed no change and for some reason titration against the other virus was not satisfactorily completed. Results of tests on those from whom at least a single specimen was tested were 2 positive to western equine alone, 2 positive to western equine and not tested for St. Louis, 1 positive to St. Louis alone and 1 to neither. From 1 infant no serum was obtained; thus there were 6 definitely diagnosed western equine infections, 3 to St. Louis virus, 2 possibly infected by both viruses, 10 who probably were not infected by either of these viruses during the illness in question, and 9 who were not adequately studied serologically.

Not 1 case of paralytic poliomyelitis was encountered, and since only 1 central nervous system infection of unknown etiology occurred in a child, we can quite safely eliminate poliomyelitis from further consideration.

The clinical picture varied widely but did not differ essentially from those cases which have been described previously from this area [1] and elsewhere.[3] One very severe case, in an adult, with recovery, has been previously reported in some detail.[4] Four infant cases were diagnosed, aged 11 days, 17 days, 5 weeks and 8 weeks. Despite the fact that infant rates have been high in Manitoba,[5] North Dakota and neighboring states [6] and in California,[7] these are the first seen in the Yakima Valley among 130 cases. Case histories are given for 1 of the youngest infants, for a 9 year old boy with a very severe St. Louis infection and for 2 adults with typical, moderately severe disease manifestations, 1 due to the western equine virus and 1 with unknown etiology:

Case 11.—L. H., a girl, was born July 27 in a Yakima hospital and went home with her mother on July 30 to a poorly screened, mosquito infected home at the edge of the city. There were 8 siblings, all apparently well. The home was adjacent to irrigated pasture and orchard land and was within half a mile of a mill pond. There was a horse with encephalitis in a nearby pasture at about this time. Within 150 yards there were horses, mules, cows, pigs, goats, dogs, cats, rats, mice, chickens, turkeys and ducks. The father recalled killing an engorged mosquito on the infant on August 11. On August 13, fourteen days after coming from the hospital, the infant vomited several times and continued to do so the next two days. Fever was noted on the second day, and the child was taken to a doctor. Convulsions began to occur that day. She was hospitalized on the 16th. The highest recorded temperature, 104.6 F., was on admission at 4 p. m. Convulsions occurred frequently, beginning usually with left sided twitching, progressing slowly to convulsions involving both sides, with extreme deviation of eyes to the right. During and after the convulsions there was cyanosis, and the infant was decidedly spastic at all times. Any attempt to flex the neck or a limb would stimulate another convulsion. The temperature fell slowly to 100 F. on the morning of the 17th but rose to 104.2 F. again that evening, fell to 100.4 F. the following morning and then rose to 102 F. that evening. It was essentially normal that night and remained at a normal level.

On the 17th a lumbar puncture revealed an increased pressure, 478 cells, of which 82 per cent were polymorphonuclears, and an increase in globulin. No organisms were seen in the smear of the centrifuged sediment. Enough fluid was removed to bring the pressure to a normal level. The following day another puncture was made, but blood prevented a suitable count. The pressure was still elevated. At this time the red cell count was 3,860,000 and the leukocyte count 25,800. Convulsions continued without much change until the sixth day of hospitalization. Definite general improvement was then noted, and the formula was voluntarily taken. Treatment in addition to lumbar punc-

2. Meiklejohn, Gordon, and Hammon, W. M.: Epidemic of Encephalitis, Predominantly St. Louis Type, in Pinal County, Arizona, J. A. M. A. **118**: 961-964 (March 21) 1942. Hammon.[1]

3. Hammon, W. McD.: The Epidemic Encephalitides of North America, M. Clin. North America **27**: 632-650 (May) 1943. Meiklejohn and Hammon.[2]

4. Hammon.[3]

5. Jackson, F. W.: Encephalitis (Western Equine) in Manitoba, 1941, Am. J. Pub. Health **33**: 833-838 (July) 1943.

6. Leake, J. P.: Epidemic of Infectious Encephalitis, Pub. Health Rep. **56**: 1902-1905 (Sept. 26) 1941.

7. Howitt, Beatrice F.: Virus of Equine and of St. Louis Encephalitis in Relationship to Human Infections in California, 1937-1938, Am. J. Pub. Health **29**: 1083-1097 (Oct.) 1939. Buss, W. C., and Howitt, Beatrice F.: Human Equine Encephalomyelitis in Kern County, Calif., 1938-1939 and 1940, ibid. **31**: 935-944 (Sept.) 1941. Howitt, Beatrice F.: Human Equine Encephalomyelitis and St. Louis Encephalitis in California 1939-1940, ibid. **32**: 503-515 (May) 1942.

ture consisted in repeated parenteral administration of glucose and saline solution, sulfapyridine and gavage feedings. Discharge was on the eleventh hospital day, at which time the infant seemed entirely normal. Blood serum taken August 20 (the seventh day after onset) protected against the western equine virus only when undiluted. Serum on the 27th (the fourteenth day after onset) protected in a dilution of 1:125 at least (highest dilution tested). This serum failed to protect against the St. Louis virus.

CASE 3.—R. S., aged 9, was a normally developed boy from a rural home. There were no other recognized cases in the vicinity and relatively small numbers of mosquitoes were found breeding nearby, but these were principally Culex tarsalis, collected from the chicken houses. His mother knew of only occasional mosquito bites. In the immediate vicinity there were horses, mules, cows, pigs, dogs, cats, rats, mice and large numbers of chickens. On July 26 he first complained of headache and abdominal pain and was found to have a temperature of 100 F. A physician examined him, found a red throat and bilaterally. The bladder was greatly distended, though he had been catheterized a few hours before. His breath was fetid and he was perspiring profusely. Lumbar puncture revealed a pressure of 28 mm. of mercury, and the clear fluid obtained had 164 cells per cubic millimeter, 40 per cent of which were polymorphonuclears. The globulin test was reported normal, and culture was negative. The red cell count was 4,760,000, with 90 per cent hemoglobin, and the white cell count was 11,000, 84 per cent of the leukocytes being polymorphonuclear and 15 per cent lymphocytes. The course of the illness was prolonged and very severe. The temperature ranged for the first two hospital days between 103.9 and 105.2 F. (all rectal). By the sixth hospital day it fell to 101.2 F. and remained between that and 102 F. till about the thirteenth day, then occasionally reached normal but was slightly elevated almost every day for well over a month. He remained comatose and with frequent convulsions until August 3 (the sixth hospital day), when he regained consciousness for a few moments. He remained spastic and required occasional catheterization. Lum-

TABLE 1.—*Patients by Age, Sex, Date of Onset, Spinal Fluid Cell Count and Results of Neutralization and Virus Tests*

					Neutralization Test					
					Convalescent Serum		Titer Increase			
Case	Age, Years	Sex	Date of Onset	Total Cells Cerebrospinal Fluid	Western Equine	St. Louis	Western Equine	St. Louis	Japanese B	Virus Test Pharyngeal Washings
11	17 days	♀	8/15	479	+	0	+	0	..	..
13	49	♂	8/17	177	+	0	+	0	..	0
6	67	♂	8/ 8	84	+	+	+	0	..	..
8	68	♂	8/ 8	58	+	+	+	0	..	..
18	5 wks.	♂	8/15	8	+	±	+*	0†	..	..
22	8 wks.	♂	8/24	200	+	+	+*	0†	..	..
10	13	♂	8/17	304	+	+	+	+	..	0
23	58	♂	8/25	115	+	+	+	+	..	0
3	9	♂	7/26	300	0	+	0	+	0	..
2	14	♀	7/10	82	+	+	0	+	..	..
24	40	♂	8/27	129	+	+	0	+	..	..
19	60	♂	8/22	107	+	0	0	0	..	..
15	35	♂	8/14	...	+	+	0	0	..	..
16	48	♀	8/21	60	+	+	0	0	..	0
17	55	♀	8/20	245	+	+	0	0	..	0
20	62	♂	8/19	...	+	+	0	0	..	..
21	21	♂	8/26	...	+	+	0	0	..	..
27	42	♂	9/ 4	46	+	+	0	0	..	..
1	23	♂	7/12	50	0	+	0	0	0	..
9	49	♀	8/10	536	0	+	0	0	0	0
4	3	♂	7/28	12	0	0	0	0	0	..
5	..	♀	8/ 6	133	+	0	..‡	..‡	..	..
14	70	♀	8/20	113	+	0	..‡	..‡	..	..
26	31	♂	8/28	38	+	..	..‡	..‡	..	..
30	71	♀	8/25	..	+	..	..‡	..‡	..	..
28	11	♀	9/ 6	75	0	+	..‡	..‡	0	..
25	68	♂	8/25	920	0	0	..‡	..‡	0	..
12	11 days	♀	8/16	183	..	..	..	..	..	..

* Single serum specimen from an infant, mother's serum negative.
† Single serum specimen from an infant, mother's serum also positive but titer much higher.
‡ Only one serum specimen tested.

treated him for a sore throat. The following day he was worse, with temperature of 102.4 F. He vomited once and complained of sore throat, dizziness and abdominal pain. The following day the temperature rose to 103.6 F. and he manifested rather pronounced drowsiness. There was, however, no more nausea or vomiting, but abdominal pain continued. The next day, July 29, he was hospitalized because he became uncooperative, irrational and staring and the temperature rose to 104.2 F. Urinary retention and dysarthria also developed. The next day tremors of the hands and jaws developed, the mental confusion first became worse, and by evening he became comatose and generalized convulsions developed. Shortly before coma and convulsions developed he was examined by one of us for the first time. His limbs showed moderate spastic resistance; his speech was garbled and incoherent. His mouth could not be opened. The pupils were regular in shape and size and reacted normally to light. He stared into space, and there was no indication that he saw anything. There was no nystagmus or strabismus. Tremor of the hands was noticeable. The neck was quite rigid, and the back moderately so. There was considerable tension in the hamstrings on both sides. No tendon reflexes could be elicited except the right knee jerk. Abdominal and cremasteric reflexes were absent. There was no Hoffman sign, but there was a positive Babinski reflex bar punctures were made almost daily, showing no change except for an increase in the proportion of lymphocytes. On August 5 and 6 he again regained consciousness temporarily and recognized and spoke to his mother once. However, on the 8th, when the temperature again reached 103.4 F., he began another two days of complete coma. By the 13th he still required tube feeding and spoke only to his parents, and his mental state was obviously still very confused. On the 15th he began to take food voluntarily and showed increased cooperation otherwise. By the end of the month he was able to sit up and was talking glibly, but he lived in a world of imagination. He was last seen that year on September 9. He was still hospitalized, still voiding involuntarily, and was incapable of remembering anything about the present. He recognized persons he knew before his illness and talked intelligently of past events but never learned a new name or face and had no concept of the time of day or memory of any event of the same day or the previous one. He was still running a low grade, daily fever. When seen just recently, two years after the acute phase, a great deal of improvement had occurred but he was far from normal. He can carry on conversation and discuss present or past events quite normally for a short period, but suddenly he will again lapse into fantastic imagination. This change is not apparent except for the incongruity of the facts

he states. He is extremely hyperactive and nervous and occasionally has epileptiform convulsions. He returned to school for a short time and in some subjects did fairly well but at recess time wandered away several times and forgot to return. During the early, acute phase of his illness, sulfonamide drugs were given and they were given repeatedly at later intervals to control exacerbations of urinary tract infection. Blood serum was taken the third, fifteenth and thirty-third days after onset. All serums failed to protect against the western equine virus and the Japanese B virus, but an increase of titer was detected to the St. Louis virus, the final titer reaching 1 : 243.

Case 13.—C. S., a man aged 49, a farmer who had lived twenty years in the Yakima Valley, his home and farm being near the southern end of the valley, on August 18, in connection with what he thought was a cold, developed a severe headache with nausea after a few hours of general malaise and coryza. He continued to work for two more days with the headache becoming progressively worse; then he vomited several times, went to bed and called a physician. After two days in bed at home he became so much worse that the physician insisted on hospitalization. On August 21, at the time of hospital admission, he was found to have a temperature of 104 F., he was flushed, the face was edematous and he was bewildered, speaking thickly and slowly with great difficulty, sometimes irrationally. He had a mild tremor of the mandible when attempting to speak. He was severely dehydrated, his breath was foul and he was sweating profusely. His pupils were regular in shape and equal in size but quite contracted even in a darkened room. Vision appeared to be normal and there was no nystagmus or strabismus. The throat was moderately injected. The tongue had a definite but fine tremor. The neck was moderately stiff and the hamstrings were tense, but the back showed almost normal flexion. All extremities were very slightly spastic. The biceps and knee jerks were present and equal, but other tendon reflexes could not be elicited. Hoffman and Babinski reactions were not elicited. Abdominal reflexes were absent and the left cremasteric could not be demonstrated. Neither scrotum contracted after pinching. The spinal fluid was clear but contained 177 cells, of which 16 per cent were polymorphonuclears. The globulin was increased. The following day, after adequate fluids had been given, the red blood cell count was 3,990,000, the hemoglobin 79 per cent and the leukocyte count 17,600, 78 per cent of the leukocytes being polymorphonuclears. During the next three days, though the temperature gradually fell to a maximum of 101.4 F., he progressively developed more severe tremors of the tongue, chin, arms and legs. However, he felt better, the headache and general malaise having decreased. His mentality also cleared during these three days. By August 28, the seventh hospital day, his reflexes were all present and normal, the edema had left the face, he was eating well and the temperature was normal. However, the tremors were still very noticeable. His only drug treatment was sulfathiazole during the acute phase as a prophylaxis against secondary bacterial invaders. He was discharged on September 13, still slightly tremorous and very easily fatigued. Serum taken on the fifth day of illness protected against the western equine virus only when undiluted, but on the twenty-fifth day it protected in a dilution of 1 : 125. Neither serum protected against the St. Louis virus.

Case 16.—A. B., a man aged 48, an orchard laborer, a resident of the valley for twelve years, living just outside a small midvalley town in a typical rural setting, with mosquitoes, chickens and other animals. On August 21 he developed a severe headache, then nausea, vomiting, dizziness, abdominal pain and feverishness later in the day. He also complained of severe pain in the legs and back. The following day he became very drowsy and noted photophobia together with intensification of other symptoms. On August 23 (the second day of illness) he was hospitalized. The maximum recorded temperature that day was 101.4 F. He appeared very drowsy and toxic, and his face was bloated. His pupils were regular in size and reacted to light but were abnormally small. Otherwise his eyes were normal. There was no tremor of the tongue or hands and the speech was normal, though slow. The neck was moderately rigid and the hamstrings were tight. The abdomen was slightly distended. All the limbs seemed slightly spastic. Biceps tendon and knee jerks were normal, but other tendon reflexes could not be elicited. There was a positive Babinski reaction on the left. Both abdominal reflexes were absent and the scrotum failed to contract on pinching, though both cremasteric reflexes were normal. The spinal fluid was clear, with 48 cells per cubic millimeter. There were 38 per cent polymorphonuclears, 50 per cent lymphocytes and 12 per cent large mononuclears. On the following day the patient was slightly worse, with the temperature up to 103.6 F. The next day he had a chill, became quite restless, tremors of the mandible and the tongue appeared and his headache was much more severe. There was a partially sustained clonus of both legs. The next day (August 26) he groaned constantly with headache and cared about nothing else. A lumbar puncture showed a slight increase in pressure and 60 cells, 96 per cent lymphocytes and 4 per cent large mononuclear. The headache was partially relieved following the tap. The maximum temperature was 101 F. He was much improved the next day, the temperature was down and all reflexes were normal. Improvement was constant and he was discharged from the hospital on September 9, seventeen days after admission. Serum taken on the second and twelfth days after onset contained a high titer of antibodies to both western equine and St. Louis virus, but no change of titer could be demonstrated. It must be supposed that the patient had serologic immunity to both of these viruses at the onset and was probably infected by another one which produced a similar clinical disease.

There were but 2 fatal cases in this outbreak, making a case fatality rate of 7.2 per cent. In 1940 and 1941 the rates were 22.4 per cent and 11.5 per cent respectively. Experience in treating the severe cases probably contributed to this reduced fatality. In 1 of the 2 fatal cases of 1942 death occurred in a nursing home on the fourth day of illness, a few hours after "half a cup" of spinal fluid was drained out. There was not enough information obtained to draw any definite conclusions as to the severity of the illness or the immediate cause of death. The other fatality was of a woman aged 70 who developed pulmonary complications on the fourth day while on inadequate sulfonamide dosage. She obviously needed continual special nursing care and it was requested, but owing to inability to obtain special nurses at the county hospital because of inadequate local supply she did not receive anywhere near adequate care and died of bronchopneumonia about forty-eight hours later. There were 6 other patients over 60 years of age who had severe disease but did recover, owing in a large part to excellent medical and nursing care. All but 1 had sulfonamides during the acute phase, probably preventing in some instances pulmonary and urinary complications.[4] Tube feeding, parenteral fluids, frequent turning and other symptomatic treatment contributed greatly. This consultant (W. M. H.) noted a pronounced improvement in the care of these cases during the three annual epidemics. The case fatality rate changes, though possibly not significant statistically, are at least highly suggestive.

Two other cases merit mention because of special interest. This consultant was called to see 1 patient suspected of having a virus encephalitis because of temporary coma, restlessness and delirium with high fever. Spinal fluid findings were negative and the temperature curve suggested malaria. The first blood smear made contained large numbers of Plasmodium falciparum parasites. This was an autochthonous case of cerebral malaria, a rather infrequent infection in the Yakima Valley. In 1 proved case of western equine infection the first symptoms appeared just after he had given blood for a transfusion. The recipient did not develop any symptoms of encephalitis.

EPIDEMIOLOGY

The age distribution of cases is presented in tables 1 and 2. It will be noted that the distribution indicates either an increased exposure or increased susceptibility at the extremes of life. The mean age is 36 years, as compared with 46 for 1940 and 25 for 1941.

The sex distribution, table 2, assists little in the interpretation of the age incidence. In most large outbreaks of the western equine infection the sex distribution of very old and very young has been equal and males predominated heavily only in the adult and "teen" age working group. Here there are 21 males and 7 females, with little difference in proportion of any age group except infancy. This discrepancy may be due entirely to chance distribution in these small numbers.

TABLE 2.—*Cases of Encephalitis by Age and Sex*

Age in Years	Number of Cases		
	Male	Female	Total
Under 1	2	2	4
1 - 4	1	0	1
5 - 9	1	0	1
10 - 14	1	2	3
15 - 19	0	0	0
20 - 29	2	0	2
30 - 39	2	0	2
40 - 49	4	1	5
50 - 59	1	1	2
60 plus	6	1	7
Unknown	1	0	1
Total	21	7	28

The geographic distribution varies but little from that observed previously. Eight patients lived in an urban area, 10 suburban and 10 rural. Only in 2 instances did the place of work differ from that of residence; 1 rural resident worked in a suburban area, and 1 suburban resident worked in the city of Yakima. Since the urban population represents about one third that of the whole county, there is little difference in the rates between urban and the combined suburban and rural rates. This is comparable to the findings in 1940, when rates were 57.5 and 62.7 per hundred thousand respectively. Nevertheless, when cases are plotted on a map the urban distribution is shown to be largely at the periphery of the city, where conditions in regard to domestic fowl are suburban or rural in nature.

TABLE 3.—*Cases of Encephalitis by Time of Onset*

Time in Weeks	Cases
July 10 to 16	2
17 to 23	0
24 to 30	2
31 to August 6	1
August 7 to 13	3
14 to 20	9
21 to 27	8
28 to September 3	1
September 4 to 10	2
Total	28

Seasonal distribution, as previously mentioned, and shown in chart 1 and table 3, is almost identical to that of previous years. The peak occurred during the middle and latter part of August. Quantitative mosquito studies made by Mr. W. W. Yates of the Portland office of the Bureau of Entomology and Plant Quarantine, Division of Insects Affecting Man and Animals, U. S. Department of Agriculture (under the direction of Mr. C. M. Gjullin), by using five New Jersey type light traps, showed that the activity of Culex tarsalis again correlated well with the epidemic curve[8] (chart 2). The period of greatest activity of several species, including Culex tarsalis, just preceded the peak in onset dates of human cases, a period representing probably the incubation period in man and mosquito.

MOSQUITO AND "RESERVOIR"[9] FOWL STUDIES

During the preceding year five strains of western equine virus and three of St. Louis virus were isolated from 4,655 Culex tarsalis mosquitoes tested from this area.[10] Since no virus was isolated from any other arthropod tested the previous year, the survey was limited to mosquitoes in 1942. During July and August a total of 24,751 mosquitoes, including nine species, were collected and tested for virus content, yielding forty-nine strains of virus. Of these mosquitoes 9,466 were Culex tarsalis. Results of the tests are presented in table 4. A total of forty-five viruses was isolated from this species, forty-one western equine and four St. Louis strains. Thus, in Culex tarsalis an infection rate was demonstrated of at least 1 in each 210 collected, as compared to 1 in each 386 found the preceding year. The role of Culex tarsalis as a natural vector of these viruses in the Yakima Valley is thus amply confirmed. In addition to the isolations of virus from Culex tarsalis, one strain each of western equine and St. Louis virus was isolated from Culex pipiens. Strains of western equine virus were isolated from Culiseta inornata and Anopheles maculipennis freeborni. No virus was isolated from 7,503 Aedes mosquitoes tested.

TABLE 4.—*Viruses Isolated from Mosquitoes Caught in Summer*

Mosquito Species	Number Tested	Viruses Isolated		
		Western Equine	St. Louis	Total
Culex tarsalis	9,466	41	4	45
Culex pipiens	967	1	1	2
Culiseta inornata	1,950	1	0	1
Anopheles maculipennis freeborni	4,496	1	0	1
Aedes dorsalis	4,866	0	0	0
Aedes vexans	2,513	0	0	0
Aedes nigromaculis	124	0	0	0
Anopheles punctipennis	307	0	0	0
Culiseta incidens	62	0	0	0
Totals	24,751	44	5	49

An interpretation of the significance of these virus isolations by consideration of the vector abilities of the different species concerned leads to interesting conclusions. Culex tarsalis has been demonstrated to be an efficient vector of both western equine[11] and St. Louis viruses.[12] It feeds predominantly on fowl

8. Hammon, W. M.; Reeves, W. C.; Brookman, B., and Gjullin, C. M.: Mosquitoes and Encephalitis in the Yakima Valley, Washington: V. Summary of Case Against Culex Tarsalis Coquillett as a Vector of the St. Louis and Western Equine Viruses, J. Infect. Dis. **70:** 278-283 (May-June) 1942.

9. Reservoir animal is used here and elsewhere in this paper when in quotations in a restricted sense. All known vertebrate sources of these viruses are infectious for only a short time and thus are not reservoirs in the usual sense of an animal having a latent or chronic infection which may serve as a source of infection over a long period. No such a true reservoir for these viruses is known as yet. Such a reservoir, if it exists, might be vertebrate or invertebrate.

10. Hammon, W. M.; Reeves, W. C.; Brookman, B., and Izumi, E. M.: Mosquitoes and Encephalitis in the Yakima Valley, Washington: I. Arthropods Tested and Recovery of Western Equine and St. Louis Viruses from Culex Tarsalis Coquillett, J. Infect. Dis. **70:** 263-266 (May-June) 1942.

11. Hammon, W. M., and Reeves, W. C.: Laboratory Transmission of Western Equine Encephalomyelitis Virus by Mosquitoes of the Genera Culex and Culiseta, J. Exper. Med. **78:** 425-434 (Dec.) 1943.

12. Hammon, W. M., and Reeves, W. C.: Culex Tarsalis Coquillett a Proved Vector of St. Louis Encephalitis, Proc. Soc. Exper. Biol. & Med. **51:** 142-143 (Oct.) 1942; Laboratory Transmission of St. Louis Encephalitis Virus by Three Genera of Mosquitoes, J. Exper. Med. **78:** 241-253 (Oct.) 1943.

and occasionally on mammals. It becomes readily infected by feeding on fowls at a time when virus is present in the blood, and specimens thus infected become, in turn, infective by their bite after a suitable extrinsic incubation time at high temperatures.[13] Thus, it would appear that this species is an important vector of both western equine and St. Louis viruses.

Culex pipiens was found infected this year with St. Louis and western equine viruses. This species also acts as a laboratory vector of St. Louis virus [14] and thus can now be considered an established natural vector. However, in all laboratory tests this species has lost every detectable trace of western equine virus in twenty-four hours.[15] It would appear that the recovery of western equine virus from a mosquito of this species, in nature, was an instance of finding a specimen recently engorged on an infected "reservoir" animal, and the virus would probably have disappeared within a few more hours.

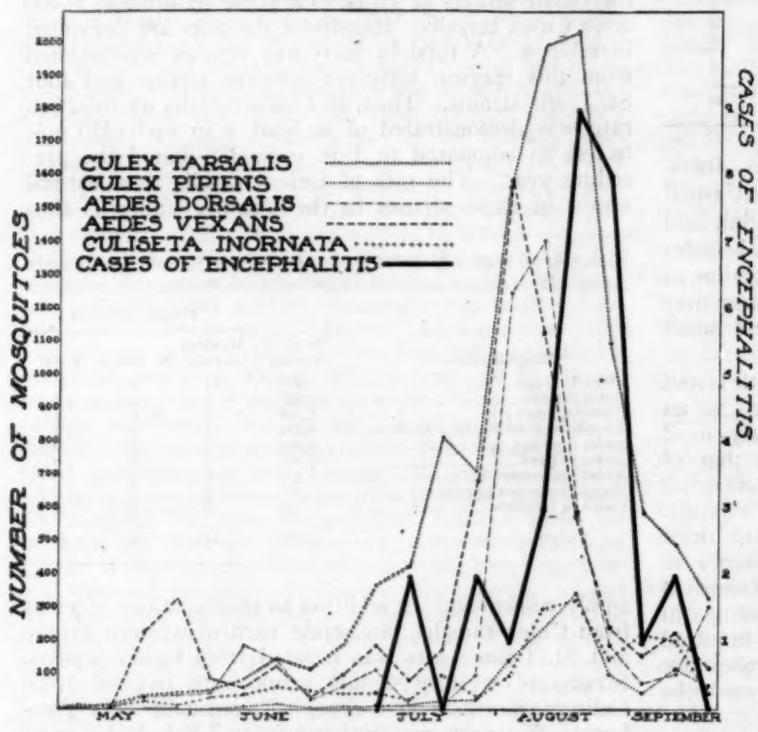

Chart 2.—Principal species of mosquitoes caught in light traps and human cases of encephalitis, by weeks.

Culiseta inornata, found infected with western equine virus, is capable of acting as a vector in the laboratory [11] and if present in large numbers might serve as a vector of importance.

Anopheles maculipennis freeborni, found infected with western equine virus, has been demonstrated to lose all detectable virus within twenty-four hours.[11] Thus, this species, like Culex pipiens, was infected in nature but apparently would not have become infectious by its bite.

Culex pipiens (St. Louis) and Culiseta inornata (western equine), the potential vectors other than Culex tarsalis which were found infected, were present in comparatively small numbers (chart 2) and could be of but small importance.

No virus other than western equine and St. Louis types was isolated from any source during the investigations.

During the survey of the previous year (1941) a small scale study was made of the feeding habits of Culex tarsalis.[16] This study was made by application of the precipitin test technic and by direct observation. This phase of the problem was greatly enlarged in the 1942 study, to throw more light on probable vertebrate reservoirs and in an attempt to discover why excellent laboratory vectors like Aedes were not found infected. A large series of blood engorged specimens, collected in domestic habitats, were tested by means of the precipitin method to determine the relative proportions which fed on domestic animal "reservoirs" of these infections and on man.[17] At the same time, hand collections were made on the horse, cow and man to determine which of the various mosquito species fed on these hosts. It was found that Culex tarsalis, the species best fitting the epidemiologic picture as a mosquito vector of encephalitis in this area, fed frequently on birds (45.7 per cent of all tested) and included most of the common domestic animals in its feeding range. The feeding habits of this species alone could result in the incidence of encephalitis antibodies demonstrated in domestic animals and man by means of the neutralization test.

Other species which were rarely or never found infected in nature appeared to be those which fed almost exclusively on large mammals (Aedes dorsalis, 96.6 per cent) which, if all like the horse, have low titers of virus in the blood, probably too low to permit infection of the mosquito.

Culex pipiens was the exception, as it fed almost exclusively on fowl. This species can now be considered a natural vector of St. Louis virus, probably important in the St. Louis area but, because of small numbers, not important in the Yakima Valley.

The results of the precipitin tests, and the repeated isolations of virus from Culex tarsalis, together with previous evidence from a serologic survey [18] give strong support to the probability that domestic fowl are an important "reservoir" of infection in the Yakima Valley. In the laboratory, the blood of domestic fowl (chickens) has been shown to serve as an excellent source of virus to infect mosquitoes.

In order to determine, if possible, whether encephalitis viruses are carried through the winter by hiber-

13. Hammon, W. M.; Reeves, W. C., and Gray, M.: Mosquito Vectors and Inapparent Animal Reservoirs of St. Louis and Western Equine Encephalitis Virus, Am. J. Pub. Health **33**: 201-207 (March) 1943.

14. Mitamura, T.; Ajamada, S.; Hazato, H.; Mori, K.; Hosoi, T.; Kitaoka, M.; Watanabe, S.; Okobu, K., and Tenyin, S.: Ueber den Infektionsmodus der epidemischen Enzephalitis, Tr. Jap. Path. Soc. **27**: 573-580, 1937. Reeves, W. C.; Hammon, W. M., and Izumi, E. C.: Experimental Transmission of St. Louis Encephalitis Virus by Culex Pipiens Linnaeus, Proc. Soc. Exper. Biol. & Med. **50**: 125-128 (May) 1942.

15. Merrill, M. H.; Lacaillade, C. W., and TenBroeck, C.: Mosquito Transmission of Equine Encephalomyelitis, Science **80**: 251-252 (Sept. 14) 1934. Hammon and Reeves.[10] Hammon, W. M., and Reeves, W. C.: Unpublished results.

16. Bang, F. B., and Reeves, W. C.: Mosquitoes and Encephalitis in the Yakima Valley, Washington: III. Feeding Habits of Culex Tarsalis Coq., a Mosquito Host of the Viruses of Western Equine and St. Louis Encephalitis, J. Infect. Dis. **70**: 273-274 (May-June) 1942.

17. Reeves, W. C., and Hammon, W. M.: Feeding Habits of the Proved and Possible Mosquito Vectors of Western Equine and St. Louis Encephalitis in the Yakima Valley, Washington, Am. J. Trop. Med. **24**: 131-134 (March) 1944.

18. Hammon, W. M.; Lundy, H. W.; Gray, J. A.; Evans, F. C.; Bang, F., and Izumi, E. M.: A Large Scale Serum Neutralization Survey of Certain Vertebrates as Part of an Epidemiological Study of Encephalitis of the Western Equine and St. Louis Types, J. Immunol. **44**: 75-86 (May) 1942.

nating mosquitoes, 5,973 such mosquitoes were collected in the Yakima Valley during January 1943 while snow was on the ground and the temperatures ranged down to minus 15 F. All tests for virus were negative. Only 18 Culex tarsalis could be found, but of Culex pipiens there were 4,789, of Anopheles 1,161. Culex pipiens and Anopheles undoubtedly winter predominantly as adults, but although Culex tarsalis has been reported to do so, it seems quite possible from our observations that some other mechanism of overwintering may be more important in this area. This may have an important bearing on the epidemiology of the disease. All our attempts so far, however, to obtain evidence of transovarian infection in Culex tarsalis of both viruses have been entirely negative.

At the end of the season to determine roughly infection rates of the two viruses in chickens, which we consider very important sources of mosquito infection, serum was drawn from 20 chickens from the spring hatch of 1942. Six definitely had antibodies to the western equine virus, and 5 had low titers in a questionable range. To the St. Louis virus only 2 had any protective power, and these fell in the questionable range. This proportion is comparable to the infection rates found in mosquitoes, 44 western equine, 5 St. Louis, indicating considerable preponderance of the western equine virus during the season in question.

SUMMARY

1. In the fourth and last of a series of annual epidemics of encephalitis in the Yakima Valley, diagnosis was accepted in 28 cases. Titration of antibodies in acute and convalescent phase serums established the diagnosis of western equine or St. Louis encephalitis in 11, 10 clinically similar cases failed to develop an increase in titer to either and so are attributed to a hypothetical third virus, and the others were not so completely studied serologically. Six serums were tested for antibodies to Japanese B virus, with negative results.

2. Maternal transmission of St. Louis virus antibody to 2 infants occurred.

3. The case fatality rate was only 7.2 per cent. The decrease from previous years (22.4 and 11.5 per cent) is attributed in part to therapy and care.

4. The occurrence of a case of autochthonous cerebral falciparum malaria introduced an additional problem in differential diagnosis.

5. Transfusion on the day of onset from 1 patient failed to produce encephalitis in the recipient.

6. Activity of Culex tarsalis mosquitoes, as indicated by light trap collections, correlated with the epidemic wave.

7. Forty-nine strains of virus were isolated from four species of mosquitoes. From Culex tarsalis were isolated forty-one strains of western equine virus, and four strains of St. Louis virus. Infection rates in Culex tarsalis were at least as high as 1 in 210.

8. Culex pipiens was found infected with both viruses but will transmit only the St. Louis strain. It is now a proved natural vector of St. Louis virus.

9. Culiseta inornata found infected with western equine virus was demonstrated to be capable of transmitting it and so becomes a proved natural vector of the western equine virus.

10. In mosquito collections made during the winter, no virus was found. It was observed that few Culex tarsalis adults, if any, survive the severe winter in the Yakima Valley.

11. Antibody studies in the 1942 season's chickens indicated that 30 to 50 per cent had been infected with western equine virus but very few with St. Louis virus. This correlates well with the proportion of the two viruses isolated from mosquitoes.

PSYCHOSOMATIC ASPECTS OF FILARIASIS

PRESENT DAY EVALUATION

LIEUTENANT COMMANDER MEYER A. ZELIGS (MC), U.S.N.R.

Knowledge of the clinical characteristics of filariasis among Marines who have returned from the South Pacific has taken a broad step forward during the past year. A sounder appreciation of the later symptomatology and clinical course of this exotic disease, together with a continued opportunity to study its psychologic aspects, has made it possible to envisage more definitely the ultimate prognosis of such cases and has clarified many of the misconceptions which unfortunately have arisen in regard to this heretofore almost unheard of condition. This advance in medical understanding has been brought about by careful study and observation of a large group of Marines who were returned from the South Pacific because of filariasis. This report represents but a small part of the clinical and rehabilitative work which is now going on at the Marine Barracks at Klamath Falls, Ore.

The need for such a center as the Marine Barracks at Klamath Falls developed after the return to the United States of large numbers of Marines with filariasis for whom no definitive plan of treatment or observation had been worked out and in regard to whom only meager scientific data were available. Knowledge of this rather obscure tropical disease in the white man had thus far been limited to short term studies by a few observers working under a diversity of environmental conditions in the field and in the United States. The problem of the ultimate disposition of these men by the military, based on statistically sound group observations, had yet to be worked out. There was thus an important need for the development of a site and program for the study of these individuals under properly controlled conditions. And so, early in 1943, in a joint undertaking by the United States Marine Corps and the Bureau of Medicine and Surgery of the U. S. Navy, the Marine Barracks at Klamath Falls was conceived and established. Its purpose was to be twofold:

(*a*) The general rehabilitation of Marines returned from overseas with filariasis or malaria (or both).

(*b*) The careful study and investigation of the clinical, therapeutic, laboratory, animal experimental and psychologic aspects of these two diseases.

The successful accomplishment of such a project necessitated the highest degree of integration between the administrative and medical departments. A well controlled program which included a graded type of physical activity, vocational and educational courses, military training and recreational activities was inaugurated, all of which was fitted into an organized schedule

From the U. S. Marine Barracks, Klamath Falls, Ore.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

in a background of continuous medical observation. The untoward and actually deteriorating effects of improper rest and inactivity on individuals with chronic, nonincapacitating disease such as filariasis are now well understood by all who have dealt with such problems, and circumvention of this long existent therapeutic pitfall was one of the primary considerations in shaping the new rehabilitative ideology of this station. An aura of activity and vigor was to innovate the atmosphere before any clinical observations of real worth could be recorded. It will be noted that I have referred to the Klamath Falls Station as a "Marine Barracks" and not as a recuperative or convalescent center. This I have done advisedly and deliberately, for it was our purpose from the outset to establish a post which would function in a combined military, vocational and educational capacity and would in no sense resemble or be regarded as a hospital. The men at the station were not referred to as "patients"; they were officially carried on the Marine Corps roster on a full duty status, unless specifically excepted because of some concurrent disabling condition. Each man enjoyed the various benefits and privileges which are generally forthcoming to every one while on active duty (such as eligibility for promotions, awards, furloughs and living off the post if married).

All Marines sent to duty at the barracks at Klamath Falls had signs of active filariasis or a history of having had filariasis during the past two years (or malaria). Those just returned from overseas, following an initial physical examination which was performed immediately after their arrival, were allowed a thirty day (overseas) furlough and on their return from leave were again examined and classified as to the type of duty which they were to perform. Thus all men sent to Klamath Falls were immediately placed on a prepared program for the duration of their stay unless they had to be hospitalized. This was to be an active duty station in its fullest sense, despite the fact that almost 80 per cent of our complement had come as former patients from the various naval hospitals and convalescent centers. The medical department functioned in the background of this setting and as an integral part of the station. It comprised a staff of medical specialists, picked laboratory research workers and technicians, nurses and corpsmen. The hospital wards and laboratories were amply equipped with all the medical and technical facilities necessary for comprehensive treatment and research.

During the formative months of the station's development, the transition for many of the men from their former convalescent or hospital routine to one of activity was accompanied by considerable difficulty. Such individuals had become physiologically and psychologically weakened as the result of months of sedentary or convalescent existence and for a considerable time were unable to meet the physical demands which this active routine required. The psychosomatic reactions to this change lasted for a few months, during which time the daily sick call was full to overflowing (at one time reaching as high as 12 per cent of the total personnel) with complaints of fatigue, fear of collapse and sundry inabilities to perform the seemingly arduous duty now required of them. Symptoms referable to sites of old injuries or disease which had been quiescent or healed for many months were psychologically brought to light and reactivated. Among these were headaches, backache, diverse gastrointestinal complaints (especially vomiting) and a host of other psychosomatic disturbances. As the training program developed, however, and the intractably psychoneurotic and other inadequate individuals were separated out, the general attitude and group morale improved dramatically and the men became desirous of completing the prescribed three months training period. In the event of reactivations, they were observed for a longer period.

For purpose of this particular study, the total complement of the station was divided into two main groups:

(*a*) Individuals with signs or history of filariasis recently returned from overseas.

(*b*) Those similarly affected but who had been evacuated to the United States six to twelve months previously and who had been "convalescing" at various naval hospitals throughout the country.

A comparative study of these two groups was undertaken, and the attitude of each individual in the group toward his symptoms was determined by careful psychiatric appraisal. Over 500 such interviews were conducted, the examiner attempting primarily to discover the extent to which the subject's mental attitude colored or affected his ability to perform active duty. A special attempt was thus made to elicit whether individuals with filariasis, after six to twelve months in the United States as convalescents or on some type of limited duty, had developed any particular or fixed attitudes in relation to their symptoms and, if so, to what degree this acquired neurotic behavior was manifest. The element of secondary gain, which invariably arises after such a neurotic pattern has been achieved, was measured by the degree of insistence for light or limited duty. In addition to the foregoing, and of essential interest in this study, was an evaluation of the degree of anxiety in these men as evidenced by expressed fear of sterility, sexual impotence and loss of libido. Following is a summary of the impressions which were formed as a result of these interviews:

1. Individuals who had been hospitalized for at least a month (or longer) were, as a group, less capable of performing active duty as compared with those who had had similar symptoms but who had not been hospitalized for more than a few days after their return to the United States. Following treatment of presenting complaints, reassurance and the inauguration of an appropriate training and vocational program which allowed expression of natural aptitudes and interests, individuals in this group soon adapted themselves to the required active routine. In general, it was found that the longer the preceding period of inactivity, the more difficult and protracted was the return to active duty.

2. Individuals recently out of combat and exhibiting classic symptoms of war neurosis or combat fatigue (battle nightmares, startle reactions, increased tension, personality change) were but little concerned about their filarial symptoms and were especially desirous of overcoming their acute nervous disturbances.

3. Individuals whose past history showed evidence of psychoneurotic behavior before they developed filariasis almost invariably utilized their filarial symptoms to help solve preexisting neurotic needs or conflicts. Exaggeration of complaints and pronounced somatic-mindedness, in the face of negative physical findings, was especially prominent in this group. Generalized aching of muscles and joints and easy fatigability were the most common features in this group.

Demonstrable signs of filarial activity was found in less than 4 per cent of all individuals and in all cases after one or more reactivations no further incapacitating

sequelae occurred. In an earlier analysis of this same group Haviland [1] reported the degree of involvement found at the time of the initial "screening" examination as presented in table 1. It will be seen that 91 per cent of men were sufficiently free from symptoms so as not to require medical attention. Of this group 40 per cent showed "mild" involvement, which usually amounted to transient aching or swelling of an extremity or of the spermatic cord following moderate or heavy physical exertion. In many cases the complaint was entirely subjective (aching, but no evidence of swelling or redness) and as the patient became physically and psychologically adapted to his activity these symptoms disappeared. With these facts in mind, let us now compare the rate of attendance at the "filariasis clinic" during its first two months with the next four months (chart 1). One sees a progressive decline in the percentage of the station complement attending the "filariasis clinic" as the period of training ensued. It is to be emphasized, furthermore, that this decline in clinic attendance occurred during the very same months in which the total filarial complement of the station was steadily increasing as the result of the continued arrival of new cases. Despite the constant increase in the filarial complement, one sees a progressive decline in the total percentage of men attending the "filariasis clinic" as the training program continued.

TABLE 1.—*Examining Physician's Evaluation at Time of "Screening Examination"*

(Taken from Haviland)

Physician's Evaluation	Men Involved (%)
No involvement	51.0
Mild involvement	40.0
Moderate involvement	9.0
Severe involvement	0.2

TABLE 2.—*Pregnancies and Births Among Wives of Marines with a History or Signs of Filariasis*

Marital Status	Cases	Pregnancies or Births	Disturbed Sexuality (Psychic Impotence, Fear of Sterility, and So On)
Married	249	45	10
Single	657	0	17
Total cases	906	45	27

Chart 2 shows the total filarial complement of the station by months. At the present time the approximate attendance at this clinic is about 1 per cent of the station's total filarial complement (chart 1, January 1945). This trend is of real significance and is emphasized as one of the essential points of this report, for it categorically summarizes the beneficial effects which took place in these men following proper physical conditioning and the removal of unfounded psychogenic fears and apprehensions concerning the outcome of this disease. Especially prevalent among the latter was the fear of sterility and other evidences of disturbed psychosexuality.

The data given in table 2 show the incidence of pregnancies and births among wives of Marines returned to the United States with a history or signs of filariasis and were obtained during the last weeks of the three to four month training period ("final screening examination") which was done preparatory to each man's transfer to another station. This table also shows the incidence of disturbed sexuality, from any cause, among the single and married Marines under observation for filariasis. It is evident that there has been no interference with procreation (18 per cent of wives were pregnant or gave birth) and the incidence of disturbed sexuality of psychogenic origin was well within the range of normality (2.8 per cent) for any group of individuals.

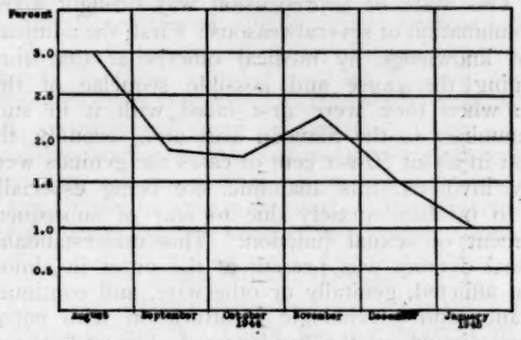

Chart 1.—Percentage of total complement of station (with filariasis) attending "filariasis clinic."

COMMENT

It appears thus, from the data presented, that the disease filariasis in a nonendemic area has a definite tendency to burn itself out after one or more reactivations. The precise mechanism for this is still under dispute by pathologists, though it is felt by most investigators [2] that the symptoms of reactivation (characterized clinically by mild fever, localized redness and swelling, retrograde lymphangitis and regional lymphadenitis) are caused by the ultimate development of an adult worm, which, having grown to its full size, creates an obstructive, inflammatory reaction in the lymphatic channels in which it is lodged and then dies and disintegrates, the latter process accounting for the acute clinical signs. Whatever the exact pathologic process may be, whether it is an obstructive one or a local allergic phenomenon or both, has yet to be determined accurately. The essential point in regard to the problem under discussion is that in individuals so affected, when removed from endemic areas, the disease runs a self-limited course and soon dies out. This categorical statement is one which until now could not be unequivocally made, because of the lack of adequate clinical data which are now at hand.

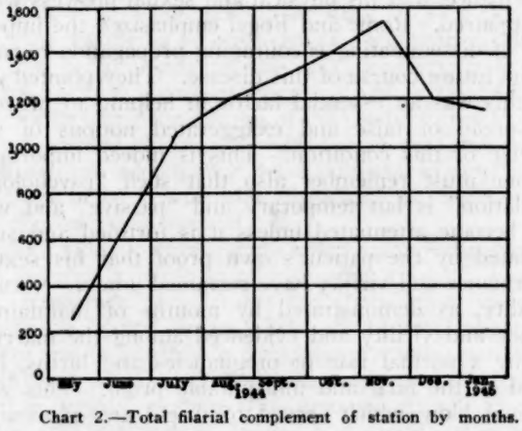

Chart 2.—Total filarial complement of station by months.

1. Haviland, J. W.: Recent Experiences with Filariasis, Northwest Med. **43**: 371-376 (Dec.) 1944.

2. Zuckerman, S. S., and Hibbard, J. S.: Clinicopathologic Study of Early Filariasis, U. S. Nav. M. Bull. **44**: 27-36 (Jan.) 1945.

Factual knowledge, such as this, has proved of immense importance in the therapeutic handling of these and more recently arrived cases. Just a year ago Rome and Fogel,[3] in a then timely article, discussed the keen and almost universal anxiety which was seen to be associated with this disease soon after its inception. This state of apprehension was brought about by a combination of several reasons: First, the admitted lack of knowledge by medical officers at that time concerning the cause and possible sequelae of this disease when they were first faced with it in such large numbers in the Samoan area and, secondly, the fact that in about 50 per cent of cases the genitals were initially involved, this anatomic site being especially prone to produce anxiety due to fear of subsequent impairment of sexual function. This understandable emotional overlay was present at the onset in almost all men afflicted, genitally or otherwise, and continued observance and psychologic identification with native Samoans (in whom the incidence of obvious "mumu" or gross elephantiasis in some villages ran as high as 85 per cent) served to enhance and maintain the unwholesome state of mind. In many of the more suggestible, imaginative and psychologically susceptible ones, as Rome and Fogel go on to point out, actual mental depression occurred. In others, psychic impotence and profound fear of sterility developed after their return to the United States. Such psychosomatic manifestations no longer obtain, however, and this brings us to the present day evaluation of this aspect of the problem. From a clinical and statistical review of the group of patients in this study it can now safely be said that the initial anxiety concerning the outcome of this disease, such as impairment of sexual function and the development of elephantiasis of limbs or scrotum, is no longer present. Only in previously psychoneurotic or constitutionally inadequate individuals is there still evidence of such worries and fears. It is to be further emphasized that the regimen which was used to overcome this state of apprehension included a program of prophylactic psychiatry which was soon replaced by the subject's own appreciation, in terms of actual performance, that his physical and sexual prowess were not impaired. Rome and Fogel emphasized the importance of disseminating encouraging propaganda regarding the future course of this disease. They pointed out that this was an essential factor in helping to prevent the spread of false and exaggerated notions of the sequelae of this condition. This is indeed important, but one must remember also that such "psychologic inoculation" is but temporary and "passive" and will soon become attenuated unless it is fortified and substantiated by the patient's own proof that his sexual performance and virility have remained intact. Normal sexuality, as demonstrated by months of maintained potency and virility and evidenced among the married men by a normal rate of pregnancies and births, has served as the final and indisputable proof. This was the final blow which served to dispel any remaining apprehension in this regard.

CONCLUSIONS

The following conclusions concerning the course, prognosis and psychosomatic features of patients with filariasis derive from this study:

1. Following removal of individuals afflicted with early signs of filariasis from the endemic area, the disease has been shown to run a self-limited course and, after one or more clinical reactivations, burns out.

2. The rehabilitation and restoration to full duty of individuals with signs or a history of filariasis is in a large measure dependent on a combined program of military, vocational, educational and medical training and supervision, this being of especial significance in the handling of men previously weakened by prescribed inactivity.

3. No demonstrable impairment of sexual function, either libidinous or procreative, has resulted from this disease.

4. Severe or incapacitating sequelae have thus far occurred in only 0.2 per cent of persons with filariasis.

5. The clinical, military and psychologic import of this wouldbe problem should, within another year or so, have entirely disappeared.

3. Rome, H. P., and Fogel, R. H.: The Psychosomatic Manifestations of Filariasis, J. A. M. A. **123**: 944-946 (Dec. 11) 1943.

FILARIASIS

EARLY CLINICAL MANIFESTATIONS

AN ANALYSIS OF THIRTY-FIVE CASES

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Filariasis is a tropical disease endemic in many parts of the world that are now inhabited by American troops. In its importance among mosquito borne diseases it looms second only to malaria. However, unlike malaria, the importance of filariasis as a military medical problem has not been fully evaluated as yet because of its long incubation period, estimated to last as long as two years. It is only recently that American military personnel stationed in endemic areas have reached the end of this incubation period. A proper evaluation of the problem should therefore soon become apparent.

Filariasis, moreover, may well constitute an important future civilian medical problem. Theoretically, any soldier returning from an endemic area may develop filariasis two years hence when he may well have returned to civilian life. It becomes obvious, therefore, that physicians throughout the United States may be called on to recognize early manifestations of filariasis.

This report is based on the observation of 35 cases admitted to a station hospital of the South Pacific Forward Area and presenting a symptom complex suggestive of early filariasis.

It is readily conceded that the final proof for the diagnosis, the demonstration of Filaria bancrofti or its larvae, was missing in all cases. Repeated thick blood smears taken at different hours of the day and night failed constantly to reveal microfilariae. This observation is in accord with many attempts in large numbers of similar cases.[1]

A great deal of work is being done at present to devise laboratory methods helpful in the diagnosis of early filariasis. Such tests as skin tests and immunity reactions either are in the experimental stage or have failed to prove their usefulness.[2] It appears, therefore,

1. Burhans, R. A.; Camp, J. D.; Butt, H. R., and Cragg, R. W.: Lymphangitis of Suspected Filarial Origin: A Preliminary Report Concerning Its Treatment, U. S. Nav. M. Bull. **42**: 336 (Feb.) 1944. Rome, H. P., and Fogel, R. H.: The Psychosomatic Manifestations of Filariasis, J. A. M. A. **123**: 944 (Dec. 11) 1943. Michael, P.: Filariasis Among Navy and Marine Personnel: Report on Laboratory Investigations, U. S. Nav. M. Bull. **42**: 1059 (May) 1944. Fogel, R. H., and Huntington, R. W., Jr.: Genital Manifestations of Early Filariasis, ibid. **43**: 263 (Aug.) 1944.

2. Dickson, J. G.; Huntington, R. W., and Eichold, S.: Filariasis in Defense Force, Samoan Group, U. S. Nav. M. Bull. **41**: 1240 (Sept.) 1943. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 6, Philadelphia, Blakiston Company, 1942.

important to depend on a clinical picture which should be sufficiently characteristic to permit a diagnosis of early filariasis.

Current textbooks [3] offer a great deal of information on the later stages of the disease, such as the febrile filarial attacks and the final chronic stage, the elephantoid type of the disease. However, information as to the early stage of the disease, immediately following the incubation period, is scanty. It is this stage which at this time presents a pressing problem for medical officers serving in tropical and endemic areas. Such a stage of early filarial disease has been described as a latent symptomless period which follows the incubation period and which may last for several years or even throughout life. There are said to be typically no manifest symptoms, although local tissue alterations around the adult worms may be in progress.[4]

My observations would bear out the fact that early filarial disease is not as symptomless as formerly believed and that a rather well defined clinical picture presents itself, sufficiently typical to suggest the presence of the disease. The characteristic salient features of 35 cases are herewith described.

CLINICAL HISTORY

The clinical history was significant in many respects. All soldiers came from an area known to be heavily infested with Filaria. They were exposed to day and night biting mosquitoes. At times they were assigned to night duty, such as night guard duty, night repair crews and unloading ships.

Under the assumption that the time of their arrival at the endemic area was identical with the time of exposure, the incubation time in this series of cases lasted from three to six months. After this period symptoms became noticeable. All patients were hospitalized from one to three months after onset of symptoms. The clinical syndrome described herein would represent, therefore, a stage of filariasis which appears four to nine months following exposure.

The disease started slowly and progressed gradually with intermissions. The most frequently described early symptom was a feeling of numbness or weakness in a leg or an arm. Frequently the affected extremity would "fall asleep," particularly at night, disturbing the patient's sleep. This was shortly followed by an aching sensation in one or more extremities, particularly after heavy work. Gradually the ache developed into a frank pain which was keenly felt during the rest period immediately following heavy exertion. The pain usually originated in the axilla or groin and it was then that the men discovered the presence of axillary or inguinal lymphadenopathy.

As time progressed any mild exertion such as a brisk walk would elicit pain in the affected parts. Eventually a certain periodicity became unmistakable. With or without preceding exertion, periodically recurring pains around the axilla, arms, groins, thighs and scrotal regions were described, occasionally accompanied by visible swellings, particularly around the groin and scrotal regions. The duration of these periodic attacks was described as lasting from a few hours to several days, followed by periods of days or weeks of well being. Nocturnal occurrence of the attacks was frequently observed, and even in the quiet periods of intermission nocturnal pains of various degree were noted. This was especially true of nightly recurring testicular pains. Such nocturnal orchiodynia was experienced so commonly that it constituted an important part of the patient's history. Finally the patients became aware of the constant presence of palpable nodes, notably around the groins and scrotal regions, although periodic changes in the degree of such enlargements were common.

Such a history usually covered a period of from four weeks to three months prior to hospital admission. None of the patients gave a history as to involvement of constitutional signs or symptoms such as general malaise, headaches or loss of weight, strength or appetite. In fact, general well being was usually emphasized. Only 1 patient gave a history of fever during attacks of pain, and this was verified by hospital observation.

PHYSICAL FINDINGS

Physical examination disclosed all patients in good general condition. There was no evidence of weight loss, debility or anemia. Cardiovascular, respiratory and gastrointestinal systems were found normal throughout. Pathologic findings were strictly confined to the lymphatic and genital system.

Involvement of the lymphatic apparatus was characterized by a more or less generalized lymphadenopathy, which was present in all of the 35 cases. The lymphadenopathy consisted of multiple slightly tender, firm well separated nodes of from pea to walnut size. There was no tendency toward confluence, attachment to skin or breakdown.

TABLE 1.—*Distribution of Lymphadenopathy in 35 Cases*

	Supraclavicular	Axillary	Pectoral	Epitrochlear	Inguinal	Femoral	Popliteal
Number of cases.....	1	35	3	11	35	35	3
Per cent.....	3	100	9	31	100	100	9

Bilateral axillary, inguinal and femoral adenopathy was present in all cases. In addition, epitrochlear adenopathy was found in 11 cases, pectoral adenopathy in 3 cases and popliteal adenopathy in 3 cases. Only 1 case presented a supraclavicular adenopathy (table 1).

The pectoral adenopathy was pronounced in all 3 cases seen, a string of lymph glands extending from the axilla along the margin of the pectoral muscle downward toward the nipple. In 1 case the pectoral and subpectoral adenopathy was pronounced and tender enough to be erroneously diagnosed as acute mastitis by the referring medical officer.

As a rule, however, acute inflammatory changes such as redness, edema and heat were absent. Episodes of retrograde (centrifugal) lymphangitis were not observed in this series. It must be emphasized that there was no noticeable correlation between periodically recurring pains and the objective appearance of glands.

The genital system was involved in all 35 cases, although degree and intensity of involvement varied greatly not only from case to case but also frequently within the individual during the period of observation.

The most frequently encountered genital involvement was a left funiculitis found in 21 cases. In 6 of these cases there was in addition a left varicocele. A right funiculitis was found in 5 cases, and in 1 additional case it was associated with a bilateral varicocele. The total number of cases presenting a varicocele was 10, a hydrocele 3 and an epididymitis 1 (table 2).

3. Manson-Bahr, P. H.: Manson's Tropical Diseases, ed. 11, Baltimore, Williams & Wilkins Company, 1943. Strong.[2]
4. Craig, C. F., and Faust, E. C.: Clinical Parasitology, ed. 3, Philadelphia, Lea & Febiger, 1943.

The diagnosis of funiculitis was based on enlargement, often of a peculiar nodular character, thickening, edema and tenderness of funicular structures. It was found best to conduct this examination with the patient in the standing position. The two funiculi were examined simultaneously by rolling them between the thumb and the index finger of both hands, thus gaining impression as to their respective enlargement, nodulation, tenderness and edema.

As a further diagnostic aid it was found useful to introduce the finger into the external inguinal ring as is done in the routine examination of hernia. This procedure always elicited pronounced tenderness or frank pain presumably due to pressure of the sensitive edematous funiculus and spermatic cord against the pubic bone.

A less reliable but frequently helpful diagnostic aid was the absence of the cremasteric reflex on the affected side. It would seem reasonable to assume that edema and infiltration of the cremasteric muscle may interfere with the muscular reflex response on stimulation.

TABLE 2.—*Distribution of Genital Lesions in 35 Cases*

	Number of Cases				Per Cent
	Right	Left	Bilateral	Total	
Funiculitis	6	21	0	27	77
Varicocele	0	9	1	10	29
Hydrocele	2	0	1	3	9
Epididymitis	1	0	0	1	3

TABLE 3.—*Laboratory Data in 35 Cases*

	Leukocytosis Over 10,000	Sedimentation Rate		Eosinophilia	
		15 to 20 Mm.	Above 20 Mm.	5% to 10%	Above 10%
Number of cases	2	6	1	9	5
Per cent	6	17	3	26	14

Little difficulty was encountered in the diagnosis of hydrocele, varicocele and epididymitis, as these conditions corresponded exactly to the well known picture due to various other causes.

LABORATORY DATA

The following laboratory tests were performed in all 35 cases: repeated thick blood smears for microfilaria and malaria plasmodia, Kahn tests, sedimentation rates, blood counts and urine examinations. In addition, biopsy of inguinal lymph glands was done in 4 cases and hydrocele fluid examinations in 2 cases.

As stated before, blood smears taken at various intervals, day and night, were consistently negative for both filarial and malarial parasites. Careful examination of aspirated hydrocele fluid revealed no microfilariae in 2 cases.

Excised lymph glands were examined histologically by Lieut. A. P. Gewanter, M.C.R., U.S.N., and Capt. A. J. Segal, M. C., A. U. S. The diagnosis made was chronic hyperplastic lymphadenitis and follicular hyperplasia respectively. No evidence of filariae was found in sections. Excised lymph glands, furthermore, were incubated in saline solution for twenty-four hours and the tissue juice examined for filariae. The results were negative.

Urine examinations as well as Kahn tests were negative throughout. Red blood cell counts and hemoglobin determinations revealed no evidence of anemia. The leukocyte count was between 5,000 and 10,000 in all but 2 cases, in which the counts were 14,050 and 13,750 respectively. The sedimentation rate was normal in 28 cases, elevated to between 15 and 20 mm. per hour in 6 cases and above 20 (29 per hour) in 1 case.

The eosinophil count was found elevated to between 5 and 10 per cent in 9 cases and elevated to above 10 per cent in 5 cases, the highest being 19 per cent in 1 case (table 3).

Because of the fact that eosinophilia in the tropics is most frequently due to worm infections, stools of patients showing eosinophilia were repeatedly examined for evidence of helminthiasis. Stool specimens were examined fresh by the concentration and zinc sulfate flotation method. The results were negative.

COMMENT

The value of the old dictum that a diagnosis of infectious disease should not be made without demonstration of the causative organism is undisputed. Yet if one was to adhere to this dictum the early diagnosis of filariasis could not be made in most cases, for microfilariae were not found in this series as well as in large numbers of similar cases.[1] If the diagnosis should be delayed until such time as microfilariae become demonstrable it might prevent the only effective measure, namely early removal of the patient from the endemic area. It would furthermore create a large reservoir of carriers on whom the mosquitoes could feed and thus cause widespread propagation of the disease.

It is for this reason that a syndrome such as outlined must be depended on in order to reach at least a tentative diagnosis.

There seems little doubt that the clinical picture described was actually due to filarial infection. It is true that the findings were not as evident as described in the textbook picture nor were there typical filarial attacks accompanied by constitutional symptoms such as fever, general malaise and prostration. On the other hand there was a history of exposure to day and night biting mosquitoes in an area where the native population was known to be heavily infected with filariasis. There was a more or less generalized lymphadenopathy and there were present various types of genital lesions. Periodic aggravations of pains and swellings, so characteristic of the later stages of the disease, were commonly observed. However, the asymptomatic stage, also peculiar to late cases, was not noted in this series. Nocturnal pains and particularly nocturnal orchiodynia were frequent complaints.

Laboratory tests as performed were of little diagnostic help with the possible exception of an eosinophilia which was present in 40 per cent of these cases. Present efforts to devise a reliable laboratory test for the diagnosis of early filariasis would constitute a real advancement if successful. Meanwhile, however, the diagnosis must be based on clinical evidence and it is hoped that the symptom complex as outlined herein may serve toward this goal.

SUMMARY AND CONCLUSIONS

1. A clinical syndrome believed to be sufficiently characteristic to permit the presumptive diagnosis of filariasis in its early stages has been observed.

2. Laboratory data were of no value in the early diagnosis, with the possible exception of an eosinophilia which was present in 40 per cent of this series of 35 cases. Microfilariae were not found.

THE RELATIONSHIP OF POSTSCARLATINAL ARTHRITIS AND CARDITIS TO RHEUMATIC FEVER

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Our purpose in this communication is to present the evidence of cardiac involvement occurring among 110 patients with scarlet fever and to correlate this involvement with rheumatic fever.

Cardiac injury, often associated with arthritis, has long been known to follow scarlet fever, but there still exists some question of its relationship to rheumatic fever. The cardiac and joint sequelae are still commonly designated as postscarlatinal carditis and arthritis without reference to this possible relationship. Many workers, on the other hand, have stressed the apparent close connection between postscarlatinal and rheumatic heart disease.[1]

It is well known that electrocardiographic abnormalities comparable to those seen in active rheumatic fever also occur during both the acute and the convalescent stage of scarlet fever. The reported incidence of such abnormalities has varied much, reaching as high as 86 per cent in the cases examined by Wickström.[2] This variation is in part due to differences in criteria for abnormal electrocardiograms employed by the different workers and in part to probable variation in host reactions.

The interpretation of the electrocardiographic changes has also varied among the different workers. Shookhoff and Taran[3] found only minor changes in the position of the RT or ST interval in 14 per cent and abnormalities in the shape and direction of the T waves in leads 1 and 2 in 10 per cent of 50 children with scarlet fever. They concluded that their findings in scarlet fever differed from those described in rheumatic fever in the comparative infrequency of abnormalities in the ventricular portion of the electrocardiogram, in the complete clearing up of all the abnormalities early in convalescence and in the absence of conduction disturbances. Wickström,[2] on the other hand, emphasized the striking similarity between the changes he observed in the electrocardiograms of patients with scarlet fever and in those with rheumatic fever but failed to comment on the possible etiologic relationship between the two diseases. Faulkner, Place and Ohler[4] observed prolongation of the PR interval beyond 0.20 second and T wave changes in lead 1 or 2 or both in 6 per cent of 171 patients. They also noted the striking similarity of the postscarlatinal electrocardiographic changes to those seen in active rheumatic fever and were doubtful whether the differences between the two conditions are fundamental. Roelsen[5] found electrocardiographic changes in 36 per cent of scarlatinal patients with arthralgia and in 26 per cent of those without arthralgia. In commenting on the possible etiologic relationship between the cardiac complications following scarlet fever and those of rheumatic fever he apparently believes that the scarlet fever patients who develop heart disease probably have both diseases, with a probable overlapping of the two conditions.

METHODS OF STUDY

In the present investigation only cases of unquestionable scarlet fever were included. All patients had typical scarlatinal rashes with postscarlatinal desquamation. Each patient was watched closely for any signs or symptoms of complications or sequelae. Routine symptomatic treatment was employed, and codeine rather than salicylates or aminopyrine was given to relieve discomfort. Sulfonamides were generally used only to combat developing purulent complications; many of the patients, however, received full therapeutic doses of sulfadiazine, together with a nose and throat spray containing 2.5 per cent sodium sulfadiazine, during postscarlatinal convalescence in an effort to clear up their streptococcic carrier states. Routine x-rays of the heart, lungs and paranasal sinuses were taken shortly after admission and when indicated thereafter.

Nose and throat cultures were made in duplicate on fresh 5 per cent sheep and rabbit blood agar plates on all patients on admission and routinely at weekly intervals during the remainder of their hospital stay or until two successive cultures were negative. The hemolytic streptococci were grouped and typed by the precipitin technic.[6] To avoid cross infections, only patients found to have the same type of group A streptococci were put together in rooms; otherwise they were strictly isolated.

Blood to determine the erythrocyte sedimentation rates and antistreptolysin and antifibrinolysin titers was obtained on admission and at weekly intervals. The erythrocyte sedimentation technic was that of Westergren;[7] the antifibrinolysin tests followed the method of Tillett, Edwards and Garner[8] as modified by Boisvert,[9] and the antistreptolysin determinations were made according to the method of Todd,[10] modified as previously described.[11]

With the subjects in the supine position, standard three lead electrocardiograms were obtained on all patients at the time of admission and at least once a week thereafter. Daily records were taken on 15 of the patients.

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

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OBSERVATIONS

In this study there were 101 males and 9 females ranging in age from 17 to 45 years, with an average of 23 years. The majority had mild attacks of scarlet fever and only a few were severely ill. None were considered critically ill during their scarlatinal infection.

TABLE 1.—*Distribution of Groups and Types of Streptococci Recovered from 110 Cases of Scarlet Fever*

Number of Cases	Group	Type	Number of Cases	Group	Type
8	A	3	3	A	19-6*
1	A	3-14*	2	A	26
6	A	6	8	A	30
1	A	6-14*	1	A	33
6	A	17	2	A	38
1	A	18	5	A	No type †
65	A	19	1	C	—

* Two types recovered from these cases. The type listed first was considered probably responsible for the scarlatinal infection.
† These strains did not type by the precipitin technic. Three proved to contain the T antigen of type 14 by the agglutination method.

Hemolytic streptococci, generally as the predominating micro-organism, were isolated in large numbers on culture from the nasopharynx in every case, and all belonged to group A except one, which belonged to group C. The distribution of the various types is shown in table 1. The group A strains recovered from 5 of the patients could not be typed by the anti-M precipitin technic; 3 of these strains, however, proved to have the T antigen of type 14 by the agglutination method. Two different types were isolated from 5 patients; in these instances, as shown in table 1, the type strain considered to have caused the patient's scarlatinal infection is listed first, and it is believed that the patient was probably carrying the second strain at the onset of his illness.

Sixty-three patients suffered neither purulent complications nor nonpurulent sequelae. During the acute phase of their scarlatinal infection 3 members of this group had mild, transitory joint pains (arthralgia) which subsided with the disappearance of fever; and at no time were there any objective signs of arthritis or other associated rheumatic manifestations in these 3 patients.

Twenty-nine patients suffered purulent complications: 12 had sinusitis, 7 peritonsillar abscess, 5 otitis media, 2 pneumonia, 2 cervical lymphadenitis and 1 both sinusitis and otitis media. Four of these also had electrocardiographic abnormalities and are therefore included in the next group. In addition, 3 others of the 29 had arthralgia during the acute febrile stage of their disease similar to that described in the 3 patients in the first group.

Twenty-two patients showed definite electrocardiographic abnormalities either during the acute stage or late in convalescence from their scarlatinal infection; and it is this group of patients who are of particular interest. The electrocardiographic changes together with other signs and symptoms of possible rheumatic activity which occurred concurrently are shown in table 2.

TABLE 2.—*The Correlation of the Electrocardiographic Abnormalities with Other Signs and*

Patient	Age	Sex	Type of Group A Streptococci Cultured from Nasopharynx	Day of Scarlet Fever on Which Complication or Sequela Appeared	Electrocardiographic Findings: Admission T Waves Lead 1	Lead 2	Lead 3	PR, Sec.	Maximum Change T Waves Lead 1	Lead 2	Lead 3	PR, Sec.	Discharge T Waves Lead 1	Lead 2	Lead 3	PR, Sec.
1	18	♂	6	4 (or less)	—	—	—	0.13	—	—	—	0.13	+	+	Isoelectric	0.16
2	20	♂	19	5	+	+	+	0.15	—	—	—	0.16	+	+	+	0.16
3	25	♂	19	4	+	+	+	0.16	+	+	+	0.22	+	+	+	0.16
4	32	♂	19	10	+	+	—	0.14	+	—	—	0.16	+	±	—	0.16
5	25	♀	19	12	+	+	+	0.16	+	—	—	0.16	+	+	Isoelectric	0.16
6	23	♂	19	27	+	+	—	0.12	±	—	—	0.12	+	+	Isoelectric	0.13
7	18	♂	3	15	+	+	—	0.12	+	—	—	0.13	+	+	—	0.12
8	21	♂	19	56	+	+	+	0.16	+	+ (Rate 130)	+	>0.20	+	+	+	0.18
9	20	♂	19	10	+	+	+	0.14	+	+	—	0.24	+	+	+	0.16
10	24	♂	19	35	+	+	+	0.16	+	+	+	0.26	+	+	+	0.16
11	18	♂	19	10	+	+	—	0.16	+	—	—	0.16	+	+	—	0.16
12	24	♂	19	30	+	+	∓	0.16	+	+	∓	0.24	+	+	∓	0.16
13	31	♂	19	24	+	+	+	0.16	+	+	+	0.26	+	+	+	0.14
14	32	♂	19	35	+	+	+	0.16	+	+	+	0.28	+	+	+	0.17
15	19	♂	19	19	+	+	—	0.12	+	∓ RT$_{23}$ depressed	—	0.19	+	+	—	0.12
16	24	♂	19	23	+	+ V. P. C.	+	0.15	+	+	—	0.22	+	+	—	0.16
17	25	♂	19	23	+	+	+	0.14	+	+	+	0.25	+	+	+	0.14
18	21	♂	19	40	+	+	—	0.20	+	+	—	0.28	+	+	∓	0.20
19	21	♂	19	28	+	+	+	0.14	+	+	—	0.22	+	+	∓	0.16
20	22	♂	19	19	+ (T waves low)	+	∓	0.14	—	— (Dropped beats)	—	0.29	+	+	∓	0.16
21‡	23	♀	17	29	+	+	—	0.16	+	+ (Dropped beats)	+	0.72	+	+	—	0.20
22	20	♂	6	19	+	+	+	0.12	+	+ (Dropped beats)	—	0.60	+	+	+	0.16

* indicates that these signs or symptoms may be attributed to the scarlatinal infection; → indicates trend of erythrocyte sedimentation rate or white blood cell count; the first figure is the lowest level attained prior to the onset of the sequela and the second figure is the highest level attained after the onset; those without arrows showed no significant change after the subsidence of the scarlatinal infection and during the sequela.
‡ This patient developed subcutaneous nodules.

Nineteen patients (4 through 22) developed their signs or symptoms of cardiac involvement during what may be designated as phase 3 of their illness; that

The first signs or symptoms of cardiac involvement appeared relatively early in patients 1, 2 and 3; that is, within the first five days of their primary streptococcic infections. Two of these patients developed inverted T waves in all three limb leads, and the other developed transient, partial heart block. In addition to showing electrocardiographic abnormalities, all 3 patients complained of mild joint pains; 2 had precordial distress, and 1 of these had also a gallop rhythm. The fever, leukocytosis and elevated erythrocyte sedimentation rates in these patients may all be attributed to their scarlatinal infections. The clinical course of patient 2 is shown in chart 1.

is, between the 10th and 56th days after the onset of their scarlet fever. In this group the temperature had returned to a normal level (phase 2) following the scarlatinal infection in all except patient 11; and in most instances the erythrocyte sedimentation rate and white blood count had returned to normal levels before the onset of the sequelae; that is, of phase 3. In most of these cases, therefore, it is possible to attribute the secondary rise in the temperature, leukocyte count and erythrocyte sedimentation rate to a complicating factor.

Seven of these 19 patients (4 through 10) had no definite clinical signs or symptoms of rheumatic activity contemporaneous with their electrocardiographic abnormalities. Four of these showed inversion of the T wave in lead 2 or in leads 1 and 2; the remaining 3 developed partial heart block. Patient 10 had a slight transient, secondary rise in temperature, leukocyte count and erythrocyte sedimentation rate associated with the electrocardiographic change, patient 9 had a brief secondary rise in temperature and patient 7 had only a transient leukocytosis. The associated increase in temperature, leukocyte count and erythrocyte sedimentation rate in patient 8 cannot be evaluated because of the appearance concurrently of coryza and cough. All of these patients appeared quite well at the time of the electrocardiographic abnormalities and, although repeatedly questioned, were without complaints. The clinical course of patient 10 is shown in chart 2.

Four patients (11 through 14) in addition to showing electrocardiographic abnormalities between the 10th and 35th days after the onset of their scarlatinal infection also complained of transient stiffness or mild pains in their joints, and 3 had accompanying malaise and anorexia. Three of them developed partial heart block and the remaining one showed an inverted T wave in lead 2. Three showed secondary increases in their erythrocyte sedimentation rates coincident with the electrocardiographic changes; 2 of whom also had transitory secondary rises in temperature and leukocyte count. The associated signs and symptoms of possible rheumatic activity in all 4 of these patients were mild and transient, and without the abnormal electrocardiograms they would have been difficult to interpret if not entirely neglected. The clinical course of patient 14 is illustrated in chart 3.

The remaining 8 patients (15 through 22) all had other signs and symptoms obvious enough to indicate the probable character of the sequela without the aid of the electrocardiogram. The associated signs and symptoms of rheumatic fever in patients 15 and 16 were, however, rather mild and transient. In the remaining patients (17 through 22) there could be little question regarding the diagnosis of rheumatic fever. All of them after making an apparently uneventful recovery from their scarlatinal infections developed secondary rises in temperature, leukocyte count and erythrocyte sedimentation rate with polyarthritis and definite electrocardiographic abnormalities varying from transient, partial heart block to heart block with dropped beats together with inversion of the T waves in all three leads. Patient 19 had signs of mitral stenosis when admitted with his scarlatinal infection; hence his attack undoubtedly represents a rheumatic recurrence. Patients 21 and 22 developed definite valvular disease while under observation and while receiving full doses of salicylates or aminopyrine respectively; 2 others, patients 15 and 17, developed soft apical systolic murmurs which were not transmitted; and in 1 of them the murmur disappeared with the subsidence in rheumatic activity. Patient 21 had typical subcutaneous rheumatic nodules. The clinical course of patient 17 is illustrated in chart 4.

Only 2 of the 22 patients showing definite electrocardiographic abnormalities had signs of or gave a history of having previously suffered from rheumatic fever or chorea. As already noted, patient 19 had definite signs of mitral stenosis on admission, although he denied having had rheumatic fever or chorea. Patient 3 gave a definite history of having had rheumatic fever in childhood, although on admission there were no abnormal cardiac findings.

Symptoms of Possible Active Rheumatic Fever Occurring in Twenty-Two Patients with Scarlet Fever

Erythrocyte Sedimentation Rate, Mm. per Hr.	White Blood Cells per Cu. Mm.	Fever, Degrees F.	Other Signs and Symptoms of Possible Rheumatic Fever: Arthritis	Gallop	Murmurs	Malaise	Precordial Pain
60 *	22,500 *	104 *	±	0	No	+ *	+
38 *	13,800 *	103.6 *	±	+	No	+ *	+
60 *	13,100 *	102.6 *	±	0	No	+ *	0
27 *	11,850 *	No	0	0	No	0	0
72 *	13,200 *	No	0	0	No	0	0
44* → 7	6,300	No	0	0	No	0	0
18 → 6	7,300 → 12,800	No	0	0	No	0	0
5 → 14	9,100 → 10,000 (Coryza and cough)	101	0	0	No	+ (Coryza and cough)	0
74 *	16,800 *	101	0	0	No	+ *	0
9 → 35	8,300 → 10,400	100.2	0	0	No	0	0
21 *	9,000	100.6 *	±	0	No	0	0
3 → 13	5,000	No	±	+	No	+	+
37 → 78	11,200 → 13,700	100.8	±	0	No	+	0
2 → 14	8,400 → 12,800	100.2	±	0	Apical systolic	+	0
2 → 37	8,500 → 16,300	102	+	0	Apical systolic	+	0
11 → 43	9,700 → 15,400	100.6	+	0	No	+	+
20 → 88	6,300 → 11,400	103.6	+++	0	Apical systolic	+	0
1 → 24	8,300 → 13,500	101.6	++	0	No	+	0
9 → 91	7,400 → 13,500	102	++	0	Mitral diastolic	+	0
8 → 116	14,200	101.8	++	0	No	+	0
54 → 116	7,700 → 10,000	100.6	++	0	Mitral systolic, aortic diastolic	+	0
33 → 116	13,700	104.8	++	0	Mitral systolic	+	0

SERUM ANTISTREPTOLYSIN O AND ANTIFIBRINOLYSIN STUDIES

A summary of the serum antistreptolysin O and antifibrinolysin determinations made in the 110 cases of scarlet fever is presented in table 3. A rise in the serum antistreptolysin O content was considered significant only if the titer increased by two or more dilutions. An increase of one dilution over that shown on admission was regarded as a doubtful increase in titer. Patients were considered to have had a definite increase in the antifibrinolysin titration only if between admission and discharge there was a difference of at least 2 degrees of resistance to lysin of their plasma clots. Increases of 1 degree in resistance were considered as doubtful rises.

The results of the antistreptolysin O and antifibrinolysin tests have been divided into three groups according to whether the patients had uncomplicated scarlet fever, whether they suffered purulent complications or had electrocardiographic changes (table 3). The number of cases is too small to draw any conclusions by comparing the results obtained in one group with those in another. The total number of patients, however, is probably large enough to allow a comparison of the results of the two tests in the entire group. Ninety-four (85.5 per cent) of the patients showed a definite increase in their serum antistreptolysin O titers, while only 68 (61.8 per cent) showed a definite increase in the resistance of their plasma clots in the antifibrinolysin test. Thirteen (11.8 per cent) and 14 (12.7 per cent) had doubtful increases in their antistreptolysin O and antifibrinolysin titrations respectively, while only 3 (2.7 per cent) had no increase in antistreptolysin O titer against 21 (19.1 per cent) for the antifibrinolysin titer. Seven (6.4 per cent) of the patients had 4 plus resistance to lysis of their plasma clots on admission, so that further degrees of resistance could not be measured. These results are essentially the same as those previously reported by Mote and Jones [12] in 124 cases of scarlet fever.

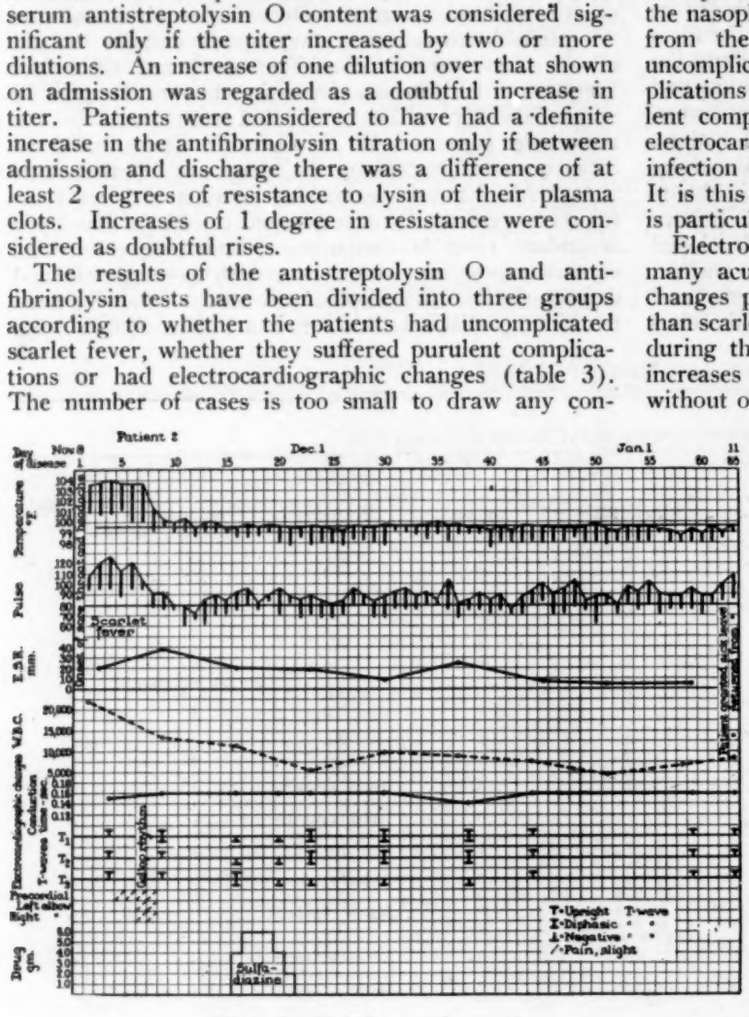

Chart 1.—Clinical course in case 2.

12. Mote, J. R., and Jones, T. D.: Studies on Hemolytic Streptococcal Antibodies in Control Groups, Rheumatic Fever and Rheumatoid Arthritis: II. The Frequency of Antistreptolysin O, Antifibrinolysin and Precipitating Antibody Responses in Scarlet Fever, Hemolytic Streptococcal Infections and Rheumatic Fever, J. Immunol. **41**: 61-85 (May) 1941.

COMMENT

An analysis of the complications and sequelae which occurred among 110 young adults with scarlet fever, who were intensively studied, has been presented. Group A streptococci were recovered on culture from the nasopharynges of 109 patients and a group C strain from the remaining one. Sixty-three patients had uncomplicated infections, 29 suffered purulent complications and 22, including 4 who also suffered purulent complications, developed definite and unequivocal electrocardiographic abnormalities, 3 during their acute infection and 19 later in postscarlatinal convalescence. It is this last group of patients with which this study is particularly concerned.

Electrocardiographic changes have been described in many acute infections,[13] including scarlet fever. The changes previously described in acute infections other than scarlet fever and diphtheria were generally observed during the acute phase of the disease, although slight increases in the auriculoventricular conduction time without other associated signs and symptoms have been noted during convalescence from pneumonia. In contrast to this, the changes noted in scarlet fever often occur late in convalescence and are frequently associated with transient joint pains, rises in temperature and leukocyte count.

It is now generally recognized that rheumatic fever is usually, if not invariably, preceded by a group A streptococcic infection (phase 1). It is also well known that there is ordinarily an asymptomatic period (phase 2) varying in length from a few days to several weeks between the acute streptococcic infection and the onset of rheumatic manifestations (phase 3). Today scarlet fever is considered a streptococcic infection. Whether the person with a streptococcic upper respiratory infection develops scarlet fever or only tonsillitis or pharyngitis seems to be determined largely by two factors; namely, the host's relative susceptibility to the erythrogenic toxin and the ability of the infecting streptococcus to produce this toxin in effective amounts. With these facts well established, it appears unreasonable to designate the symptom complex arthritis and carditis which follows scarlet fever by a different name from that applied to a similar complex which may follow tonsillitis or pharyngitis.

In view of these facts it is pertinent to consider the relationship to rheumatic fever of the condition causing the electrocardiographic abnormalities in the 22 patients considered in this study. Since the diagnosis of rheumatic fever rests on certain clinical signs and symptoms together with nonspecific laboratory evidence of infection and specific evidence of a previous hemolytic

13. Brow, G. R.: The Heart in Typhoid Fever, Canad. M. A. J. **20**: 606-608 (June) 1929. Master, A. M.; Romanoff, A., and Jaffe, H.: Electrocardiographic Changes in Pneumonia, Am. Heart J. **6**: 696-709 (June) 1931. Master, A. M., and Jaffe, H.: Electrocardiographic Evidence of Cardiac Involvement in Acute Disease, Proc. Soc. Exper. Biol. & Med. **31**: 931-933 (May) 1934. Marvin, H. M.: The Effect of Diphtheria on the Cardiovascular System: I. The Heart in Faucial Diphtheria, Am. J. Dis. Child. **29**: 433-476 (April) 1925. Porter, W. B., and Bloom, N.: The Heart in Typhoid Fever: A Clinical Study of 30 Patients, Am. Heart J. **10**: 793-797 (Aug.) 1935. Cushing, E. H.: Electrocardiographic Changes in Trichinosis, ibid. **11**: 494-496 (April) 1936. Burkhardt, E. A.; Eggleston, C., and Smith, L. W.: Electrocardiographic Changes and Peripheral Nerve Palsies in Toxic Diphtheria, Am. J. M. Sc. **195**: 301-313 (March) 1938. Fuller, C. C., and Quinlan, J. W.: Acute Pneumonitis and Pericarditis, Report of a Case, New England J. Med. **229**: 399-401 (Sept. 2) 1943. Woodward, T. E., in collaboration with Bland, E. F.: Clinical Observations in Typhus Fever, with Special Reference to the Cardiovascular System, J. A. M. A. **126**: 287-293 (Sept. 30) 1944.

streptococcic infection, we realize that the answer is not subject to experimental proof. It is generally conceded, however, that carditis is one of the major manifestations of rheumatic fever, and also that one of the most characteristic signs of active rheumatic carditis is the occurrence of electrocardiographic abnormalities. Therefore, on the basis of these two factors, all of the 22 patients have suffered an infection with an agent recognized as playing an important role in inducing rheumatic fever and also had at least one of the characteristic signs of carditis.

Without doubt 8 of these patients (15 through 22) had definite clinical evidence of rheumatic fever of varying severity. All 8 developed polyarthritis and electrocardiographic abnormalities accompanied by secondary rises in temperature, leukocyte count and erythrocyte sedimentation rate between the 19th and the 40th day after the onset of their streptococcic infection. Two, in addition, developed definite evidence of valvular disease, 1 of whom also had subcutaneous rheumatic nodules; and a third had mitral stenosis on admission as evidence of a previous rheumatic infection. Four other patients (11 through 14) differed from these 8 largely in that their rheumatic-like manifestations were milder and more transitory. All 4 had transient stiffness of the joints or mild joint pains concurrent with their electrocardiographic changes ten to thirty-five days after the onset of their scarlatinal infection; 2 in addition had slight secondary rises in temperature, leukocyte count and erythrocyte sedimentation rate; and a third had a slight increase in the erythrocyte sedimentation rate with precordial pain and gallop rhythm. Seven other patients (4 through 10) developed similar electrocardiographic abnormalities without other associated symptoms of rheumatic activity ten to fifty-six days after the onset of their scarlatinal infections. Patient 10 had a secondary rise in temperature, leukocyte count and erythrocyte sedimentation rate, while patient 9 had a brief secondary rise in temperature and patient 7 had only slight, transient leukocytosis associated with the electrocardiographic abnormalities.

From the foregoing description it is apparent that the difference between these three groups of patients is largely one of degree: it is quantitative rather than qualitative. All had a group A streptococcic infection—many with the same serologic type from the same scarlet fever epidemic—followed ten to fifty-six days later by definite electrocardiographic abnormalities of the type commonly observed in patients with active rheumatic carditis. It therefore appears most likely that the mechanism[14] by which the abnormal electrocardiograms were produced was the same in all of these patients irrespective of the occurrence of other rheumatic manifestations, and that all suffered from the same fundamental tissue injury following their streptococcic infection; namely, that characteristic of rheumatic fever.

It is somewhat more difficult to relate the changes found in the first 3 patients to those induced by rheumatic fever, largely because of the time element involved; for electrocardiographic abnormalities occur not infrequently during the acute phases of many different infections entirely unrelated to rheumatic fever. It is therefore quite possible that the early electrocardiographic abnormalities in these 3 were due to the same mechanism which cause similar abnormalities to occur in other acute infectious diseases. It is noteworthy, however, that all 3 of these patients had mild associated joint pains, 2 complained of precordial distress, and 1 of these had also a gallop rhythm. It may also be significant that 1 of the patients had previously suffered from rheumatic fever.

Mallory and Keefer[15] have recently described the histopathologic lesions in the hearts and other organs in 90 fatal cases of hemolytic streptococcic infections, including 47 cases of scarlet fever. The lesions found in the hearts of the scarlet fever patients consisted for the most part of focal accumulations of lymphocytes, plasma cells and histiocytes, at times with a few polymorphonuclear leukocytes, and a rare eosinophil. These lesions were most numerous in the subendothelial and perivascular connective tissues, which in general were the sites of the Aschoff bodies found in the control

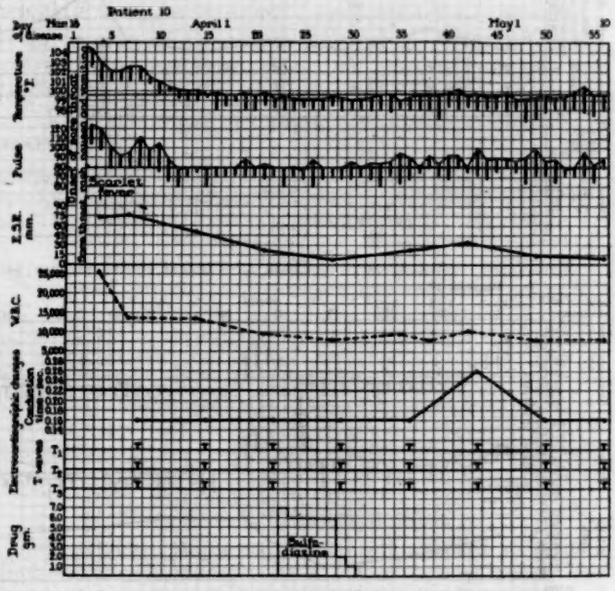

Chart 2.—Clinical course in case 10.

rheumatic hearts. Tying in with our clinical observations, it is of interest to note that these authors found these focal lesions to occur most commonly in the hearts of patients under 30 years of age who had survived their streptococcic infections for at least six to ten days. Mallory and Keefer propose the interesting hypothesis that these focal lesions may be an early stage of Aschoff body formation and present some evidence to support this concept. Similar lesions have been described by previous workers;[16] however, the interpretations of their findings have not been the same.

The cardiac abnormalities in the cases described in this study might well be explained on such a pathologic basis and may be interpreted as giving some clinical support to Mallory and Keefer's hypothesis. That is, those patients showing only transient changes late in convalescence may have had only focal collections of cells in their hearts, and these lesions then rapidly

14. We are aware that there is some evidence (Bruenn, H. G.: The Mechanism of Impaired Auriculoventricular Conduction in Acute Rheumatic Fever, Am. Heart J. **13**: 413-425 [April] 1937 and Keith, J. D.: Overstimulation of the Vagus Nerve in Rheumatic Fever, Quart. J. Med. **7**: 29-41 [Jan.] 1938) to indicate that the prolongation of the PR interval associated with active rheumatic fever may be supracardiac in origin. However, the great majority of cases described in this study presented other signs of infection, or symptoms of carditis or rheumatic fever, concurrent with the prolonged PR interval. We therefore believe that in these cases the prolonged PR interval was indicative of carditis, regardless of the mechanism by which it is produced.

15. Mallory, G. K., and Keefer, C. S.: Tissue Reactions in Fatal Cases of Streptococcus Hemolyticus Infections, Arch. Path. **32**: 334-355 (Sept.) 1941.

16. Fahr, T.: Vergleichende Herzuntersuchungen bei Scharlach, Streptokokkeninfektion und rheumatischer Granulomatose, Beitr. z. path. Anat. u. z. allg. Path. **85**: 445-468 (Nov.) 1930. Fahr.[17] Siegmund.[18] Eckert-Möbius.[19]

regressed. Those patients who in addition to the electrocardiographic changes had transient joint pains with secondary rises in temperature, leukocyte count and erythrocyte sedimentation rate may have had more numerous and more widespread lesions, possibly persisting longer and progressing to a stage more comparable with that shown by rheumatic granulomas as described by Fahr,[17] Siegmund [18] and Eckert-Möbius.[19]

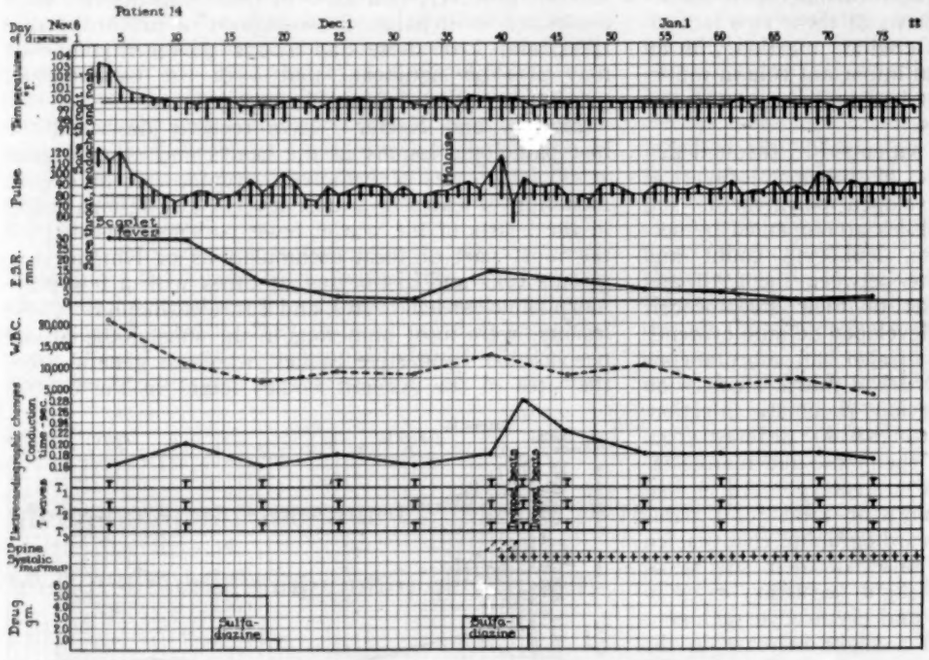

Chart 3.—Clinical course in case 14.

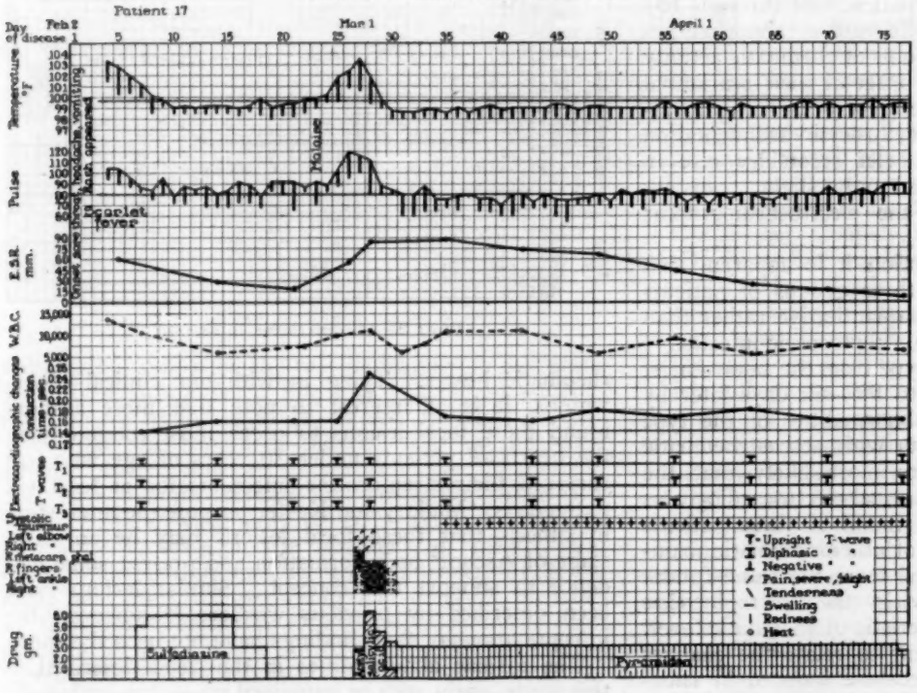

Chart 4.—Clinical course in case 17.

Those patients who had definite clinical attacks of rheumatic fever probably had comparable early lesions which, because of continued activity due to some unknown reason, in many instances progressed to form typical Aschoff bodies. Such an explanation would fit in well with our opinion that the fundamental tissue injury in all of these patients is essentially the same but that the response varies in intensity.

Whether the focal lesions described by Mallory and Keefer result from antigen-antibody reaction (allergic) in the tissues as these authors have suggested is impossible to say. Schick [20] and later Escherich and Schick [21] advanced the theory that the sequelae occurring from the end of the second week and lasting as long as seven weeks after the onset of the scarlet fever, with the greatest frequency in the third and fourth weeks, are allergic in nature. One of us [22] has previously emphasized this point of view. There is much evidence now to support such a hypothesis; namely, (1) the location and microscopic appearance of the lesions are consistent with an allergic reaction, (2) the lesions are more frequent late in the course of the disease than early and (3) similar types of lesions have been induced in rabbits by injection of foreign serums by Klinge,[23] Vaubel,[24] Junghans [25] and, more recently, Rich and Gregory.[26]

Nonpurulent arthritis or arthralgia is a well known concomitant or sequel of scarlet fever. Weaver [27] observed this complication in about 10 per cent of 5,595 cases and showed that the incidence increased with age. It was observed in 3.6 per cent of 10,000 cases at the Edinburgh City Hospital [28] and in 3.58 per cent of 153,607 cases in the Metropolitan Asylum Board Hospitals.[29] The arthritis or arthralgia may occur at any time during the course of the disease or in late convalescence. Secondary fever and leukocytosis often accompany the arthritis occurring in postscarlatinal

17. Fahr, T.: Beiträge zur Frage der Herz- und Gelenkveränderungen bei Gelenkrheumatismus und Scharlach, Virchows Arch. f. path. Anat. **232**: 134-159 (July) 1921.
18. Siegmund, H.: Veränderungen der Gefässwände und des Endokards bei Scharlach, Centralbl. f. allg. Path. u. path. Anat. **44**: 314 (Feb.) 1929.
19. Eckert-Möbius, J.: Beitrag zur Frage der Scharlachmyokarditis, Arch. f. Kreislaufforsch. **9**: 91-122 (July) 1941.
20. Schick, B.: Die Nachkrankheiten des Scharlach, Jahrb. f. Kinderh., Ergänzungsh. **65**: 132-173, 1907.
21. Escherich, T., and Schick, B.: Scharlach, Vienna, Alfred Hölder, 1912.
22. Swift, H. F.: The Heart in Infection, Tr. Cong. Am. Physicians and Surgeons **14**: 39-61 (May) 1928.

convalescence. Most observers agree that the arthritis which occurs in postscarlatinal convalescence cannot be distinguished from the arthritis associated with rheumatic fever. Actually, we believe that there is no reason to differentiate the two, because they are probably due to the same fundamental tissue injury. If frequent electrocardiograms were taken in these so-called postscarlatinal arthritis cases, a high percentage would probably show abnormal changes, as was previously observed by Roelsen.[5]

All of the patients considered in this report who developed arthritis or arthralgia late in postscarlatinal convalescence also showed abnormal electrocardiograms. Six patients in our series, however, had mild transient joint pains without electrocardiographic or other rheumatic manifestations during the early acute phase of their streptococcic infection. Whether the joint manifestations in these early cases is due to the same mechanism that produces those late in convalescence is difficult to answer at present. It is noteworthy, however, that the arthralgia seen during the acute stage of scarlet fever is rarely accompanied by evidence of exudation, such as is frequently seen with the arthritis later in convalescence. Healey[30] and Rhoads and Afremow[31] have found that a high percentage of patients developing joint pains following the injection of streptococcic erythrogenic toxin give a past history or have evidence suggestive of previous rheumatic infection. They therefore interpret their results as evidence that these individuals are sensitive to the erythrogenic toxin or other streptococcic products in the sterile filtrate injected. The mechanism of the arthralgia seen early in scarlet fever might be explained on a similar basis, but, on the other hand, it might be due to a direct toxic damage to the tissues.

Many patients with rheumatic valvular disease fail to give a history of previous attacks of rheumatic fever or chorea. White[32] estimates that a definite history of rheumatic fever can be elicited in only about 70 per cent and a history of chorea in another 5 to 10 per cent. Recently Levy, Stroud and White[33] found that 68.8 per cent of 2,250 rejected draftees with definite rheumatic valvular cardiac disease failed to recall any symptoms or signs of rheumatic fever or chorea earlier in life. Whether patients such as we have observed, with only electrocardiographic abnormalities or with associated mild arthralgia, contribute to such a "history negative" group cannot be answered at present. One might argue that they do not, because the brevity of the signs and symptoms of rheumatic carditis would hardly be expected to lead to severe and permanent valvular damage. Since we consider that these patients suffered true first attacks of rheumatic fever, we therefore believe that they should be regarded as more liable to rheumatic recurrences than normal subjects and as more likely to develop permanent cardiac damage following subsequent hemolytic streptococcic infections. Because the extent of permanent cardiac damage in rheumatic subjects is roughly proportional to the number of attacks of rheumatic fever they have suffered, it seems only logical to place this class of patients in a category to which special measures should be applied for the prevention of hemolytic streptococcic infection.

TABLE 3.—*Summary of the Antistreptolysin O and Antifibrinolysin Determinations in 110 Cases of Scarlet Fever*

Type of Case	Number of Cases	Antistreptolysin O Titer: Increased Number	Increased Per Cent	Doubtful Increase Number	Doubtful Increase Per Cent	No Increase Number	No Increase Per Cent	Antifibrinolysin Titer: Increased Number	Increased Per Cent	Doubtful Increase Number	Doubtful Increase Per Cent	No Increase Number	No Increase Per Cent	Not Measured Number	Not Measured Per Cent
Uncomplicated	63	56	88.9	4	6.3	3	4.8	38	60.3	8	12.7	15	23.8	2	3.2
Purulent complication	25*	20	80.0	5	20.0	0	0.0	15	60.0	2	8.0	5	20.0	3	12.0
Electrocardiographic abnormality	22	18	81.8	4	18.2	0	0.0	15	68.2	4	18.2	1	4.5	2	9.1
Total	110	94	85.5	13	11.8	3	2.7	68	61.8	14	12.7	21	19.1	7	6.4

* Four other patients also had purulent complications in addition to electrocardiographic abnormalities and are therefore included in the latter group.

SUMMARY AND CONCLUSIONS

The purulent complications and nonpurulent sequelae which occurred among 110 cases of scarlet fever in young adults who were intensively studied were analyzed. Group A streptococci, representing at least thirteen different types, were recovered on culture of the nasopharynges of 109 patients and a group C strain from the remaining one. Antistreptolysin O and antifibrinolysin titrations were made with the serums and plasmas respectively of all patients at weekly intervals.

Sixty-three patients had uncomplicated infections and made uneventful recoveries; 29 suffered purulent complications; and 22, including 4 who also had purulent complications, developed pronounced and unequivocal electrocardiographic abnormalities comparable with those seen in patients with active rheumatic carditis. Three of these 22 patients developed abnormal electrocardiograms during their acute streptococcic infection and the other 19 during postscarlatinal convalescence. It is this latter group of 19 patients who are of particular interest in this study.

Eight of the 19 patients who developed electrocardiographic abnormalities during postscarlatinal convales-

23. Klinge, F.: Die Eiweifsübserempfindlichkeit (Gewebsanaphylaxie) der Gelenke, Beitr. z. path. Anat. u. z. allg. Path. **83:** 185-216 (Nov.) 1929.

24. Vaubel, E.: Die Eiweifsüberempfindlichkeit (Gewebshyperergie) des Bindegewebes (II. Teil), Beitr. z. path. Anat. u. z. allg. Path. **89:** 374-418 (May) 1932.

25. Junghans, E.: Weitere Untersuchungen über die hyperergische Carditis und Arteriitis insbesondere die Aortitis, Beitr. z. path. Anat. u. z. allg. Path. **92:** 467-475 (Feb.) 1934.

26. Rich, A. R., and Gregory, J. E.: Experimental Evidence that Lesions with Basic Characteristics of Rheumatic Carditis Can Result from Anaphylactic Hypersensitivity, Bull. Johns Hopkins Hosp. **73:** 239-264 (Oct.) 1943.

27. Weaver, G. H.: Scarlet Fever, Pediatrics, edited by I. A. Abt, Philadelphia, W. B. Saunders Company, 1925, vol. 6, pp. 298-362.

28. Ker, C. B.: Ker's Infectious Diseases: A Practical Text Book, ed. 3; revised by C. Rundle, London, Humphrey Milford, Oxford University Press, 1929, pp. 116-119.

29. Rolleston, J. D.: Acute Infectious Diseases: A Handbook for Practitioners and Students, ed. 2, London, William Heinemann, Ltd., 1929, pp. 270-272.

30. Healey, C. E.: The Cause of Joint Pain Occurring During Active Immunization with Scarlet Fever Streptococcus Toxin, J. A. M. A. **108:** 628-630 (Feb. 20) 1937.

31. Rhoads, P. S., and Afremow, M. L.: The Significance of Joint Pains Caused by Sterile Streptococcus Toxin, Ann. Int. Med. **19:** 60-63 (July) 1943.

32. White, P. D.: Heart Disease, ed. 3, New York, Macmillan Company, 1944, p. 326.

33. Levy, R. L.; Stroud, W. D., and White, P. D.: Report of Reexamination of 4,994 Men Disqualified for General Military Service Because of the Diagnosis of Cardiovascular Defects, J. A. M. A. **123:** 937-944 (Dec. 11), 1029-1035 (Dec. 18) 1943.

cence had definite clinical attacks of rheumatic fever of varying severity. Four others differed from these 8 in that their rheumatic-like manifestations were milder and more transitory. The remaining 7 during a comparable period in their convalescence developed similar electrocardiographic abnormalities without other symptoms of rheumatic fever, although several had brief secondary rises in temperature, leukocyte count or erythrocyte sedimentation rate. The difference between these three groups of patients is quantitative rather than qualitative, and we believe that all suffered from the same fundamental tissue injury following their streptococcic infection; namely, that characteristic of rheumatic fever.

AN OUTBREAK OF SONNE DYSENTERY

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History indicates that bacillary dysentery is almost as old as war itself. It is said that dysentery decimated the army of Napoleon in its retreat from Moscow. Though no accurate figures are available from the Revolutionary War, there were 285,000 cases of dysentery in the federal army alone during the Civil War.

In World War I bacillary dysentery was the most important disease in the British armies in the Eastern Mediterranean area and at Gallipoli was responsible for almost 100,000 casualties. Many writers have claimed that dysentery was more important than the Turks in driving the British troops out of this area.

According to the Surgeon General's report of 1917-1918, 87,700 cases of dysentery and common diarrhea occurred among the American troops in World War I.[1] The average time lost from duty was eleven days in each case. The admission rate in 1917-1918 was 18.45 per thousand, while for the ten year period from 1930 to 1940 it dropped to 1.8 per thousand. Again in 1940-1942, with the mobilization of troops, the rate rose to 10.17 per thousand. It is apparent from these statistics that in times of war, when close congregation of large forces of soldiers is necessary, bacillary dysentery becomes one of the most important diseases encountered by the military surgeon.

World War II has been no exception. A recent report by the Preventive Medicine Division of the office of the Surgeon General,[1] which includes statistics only up to April 1942, already shows data collected on 328 outbreaks of diarrhea. Two hundred and fifty-five occurred in the continental United States and 73 abroad, affecting nearly 25,000 soldiers. Laboratory studies, made on approximately 100 of these outbreaks, indicated that roughly 50 per cent were due to one of the members of the bacillary dysentery group.

This presentation is concerned with an outbreak which occurred in a basic training center of the Army Air Forces during the summer of 1943, persisting in epidemic form for about eight weeks and then gradually tapering off.

Epidemiology revealed that the source of this outbreak began at a new target range located at some distance from the main camp but connected with it. Investigation clearly indicated that the epidemic was fly borne. Bacteriologic studies by Cohn[2] of the hospital laboratory and further corroborated by Kuhns[3] revealed the causative organism to be Bacterium sonnei. During this period of approximately four months following the onset of the outbreak, positive cultures of this organism were obtained in 181 cases.

The clinical picture of this group of cases was typical of the description found in most textbooks for the Sonne type of bacillary dysentery. By and large the cases were mild in severity. The duration of active symptoms was only three to four days. The onset in the majority of cases was sudden and the chief symptoms were chills, fever, malaise, backache and cramping abdominal pains associated with diarrhea and usually tenesmus. In most patients the diarrhea was only moderately severe, with the number of stools ranging from 2 to 20, for an average of 8 daily. The stools were watery and greenish mucoid in character in the vast majority of cases. In 10 cases (5 per cent) the stools were tinged with blood. There were no gross hemorrhages. Tenesmus was present in most of the cases but was not severe in any. Fever was present in 75 per cent of the cases admitted in the acute stage, ranging from 99 to 104 F., with an average of 101 F. Chills or chilly sensations were present in nearly 50 per cent of the cases. Although most of the patients showed some evidence of malaise or weakness, none were sufficiently prostrated from toxicity or dehydration to warrant the parenteral administration of fluids. The fever persisted as a rule for two to four days, and the diarrhea subsided after four to seven days with or without specific treatment. There were no complications and no fatalities.

On admission all patients were given bed rest, either a bland or a high protein low residue diet, and camphorated tincture of opium or morphine, depending on the severity of the diarrhea.

During the acute stage the leukocyte count varied from 6,400 to 10,000 per cubic millimeter of blood, averaging 8,200, with 62 per cent polymorphonuclear neutrophils and 37 per cent lymphocytes. It is obvious that most of these cases had perfectly normal total and differential leukocyte counts.

Sigmoidoscopy was performed in 50 cases (27 per cent) during the acute phase of the disease. The findings varied from mild to severe hyperemia and edema to granular mucosal changes and superficial ulceration. The latter occurred in only 5 cases (2.7 per cent).

The diagnosis was confirmed by culture of either fresh stool specimens, rectal swab utilizing the Hardy[4] rubber tube technic or by direct sigmoidoscopic swab. These specimens were inoculated on SS (shigella, salmonella) agar and the organism further identified by fermentative and specific serologic reactions. Emphasis should be placed on the fact that in most cases the culture reports were not available until the acute manifestations of the disease had subsided. It is clear then that any evaluation of treatment would be essentially a determination of the efficacy of various types of therapy in eradicating the carrier state.

1. Simmons, James S.: The Present State of the Army's Health, J. A. M. A. **122**: 916-923 (July 31) 1943.

2. Capt. Clarence W. Cohn, M. C., chief of the laboratory service, performed the bacteriologic studies in the cases reported.

3. Col. Dwight Kuhns, M. C., and the staff of the Fourth Service Command Laboratory, corroborated the bacteriologic findings.

4. Hardy, A. V.; Watt, J.; DeCapito, Thelma; Peterson, J., and Schlosser, E.: New Procedures in Bacteriologic Diagnosis: Carriers in Shigella Paradysenteriae; Sulfaguanidine in Control of Shigella Dysenteriae Infections, Pub. Health Rep. **57**: 521 (April 10) 1942.

As it appeared that a large number of soldiers were developing the disease, an excellent opportunity was at our disposal for the study and appraisal of existing methods of specific treatment.

The use of sulfonamides in the treatment of bacillary dysentery is not particularly new. Many reports have appeared during the past four years attesting the value of sulfonamides on the course of acute, chronic or the carrier state of bacillary dysentery. The pioneer work of Marshall and his associates [5] reported in January 1941 marked the advent of chemotherapy in bacillary dysentery when they demonstrated the value of the drug sulfaguanidine in rendering negative the stools of 15 out of 17 children affected with the disease. Since then other workers [6] have shown the value of this drug in controlling relatively large epidemics of the various forms of this disease both in the Middle East and in Puerto Rico.

In 1942 Poth, Knotts and their co-workers [7] reported on the efficacy of a newer sulfonamide, the succinyl salt of sulfathiazole, which, they reported, had a striking bacteriostatic effect not only against the usual intestinal flora but also against the strains of Shiga, Flexner and Sonne dysentery bacilli.

Hoagland, Harris and Raile,[8] in a series of 45 carriers of Bacterium paradysenteriae, divided into two groups, observed equally good results with either of the aforementioned drugs. They employed a dosage of 20 Gm. daily for six days and, regardless of the drug used, obtained 100 per cent cure of the carrier state. This work was supported by lengthy observations of cultures over a period of seventeen to sixty days.

Smyth and his associates,[9] using a similar dosage of sulfaguanidine and approximately the same dosage of succinylsulfathiazole, also observed fairly satisfactory results. However, in view of failures with each type of therapy and the potentially greater toxic effects of sulfaguanidine, they concluded that succinylsulfathiazole was the drug of choice.

Paulley,[10] in reviewing his experiences in the treatment of dysentery in the Middle East, found that sulfapyridine was more effective than sulfaguanidine in the management of acute bacillary dysentery. Unfortunately, stress of circumstances prevented complete follow-up cultures in this series.

Yannet, Leibovitz and Deutsch,[11] using plain sulfathiazole in the treatment of 27 patients suffering from Sonne dysentery, found that this sulfonamide, though producing a more rapid clinical recovery, allowed more cases to persist as carriers than those not treated in this manner.

Page,[12] in his recent report of 500 cases, 208 of which proved to be due to members of the genus Shigella, found after careful follow-up cultures 97.3 per cent cured with 130 Gm. of sulfaguanidine given in a ten day period. Page used as a secondary treatment sulfadiazine in a dosage of 22 Gm. given in a five day period and was able to render the remainder (2.7 per cent) dysentery free.

Eisenoff and Goldstein,[13] using all of the aforementioned sulfonamides except sulfapyridine in an outbreak of Sonne dysentery, found all of these agents effective in 90 per cent of the cases and eliminated the carrier state in the remaining 10 per cent by a second administration of the drug.

From this review it is evident that all of the sulfonamides have a beneficial action in acute bacillary dysentery but possess a somewhat varying effect on the eradication of the carrier state.

Since the outbreak of World War II, sulfaguanidine has attained considerable prominence in the treatment of this disease. However, it is apparent that a wide divergence of opinion exists as to the optimum dosage, with amounts varying from 4 Gm. daily for seven days [14] to as high as 20 Gm. daily for six days.[8]

Prior to 1942 little had appeared in the literature regarding the toxic effects of sulfaguanidine. Cole [15] reported a severe sulfaguanidine intoxication in a case of ulcerative colitis. He utilized a dosage of 0.1 Gm. per kilogram (roughly 6-7 Gm.) initially followed by 0.05 Gm. per kilogram (3.5 Gm.) at four hour intervals. After 110 Gm. had been given a severe intoxication developed, which was manifested by vomiting, fever, oliguria and a morbilliform rash. At the height of this reaction the blood level was only 2 mg. per hundred cubic centimeters. Recently Whyte [16] reported evidence of renal irritation in 14 out of 25 cases treated. He utilized only 9 Gm. a day for three days followed by 6 Gm. a day for four days (total dosage 51 Gm.).

Bunting and Levan,[17] reporting on the treatment of 191 soldiers with bacillary dysentery, noted objective evidence of toxicity in 11.5 per cent and subjective manifestations in 20 per cent. Crystalluria was found in 26.5 per cent, drug fever in 9.4 per cent, skin reactions in 5 cases and transient hematuria in 4. They gave 3.5 Gm. three times daily for a ten day period, a total dose of 105 Gm. They concluded that sulfaguanidine is not without its dangers and that caution in its administration should be exercised. Schnitker,[18] in reviewing the literature on the toxic manifestations of sulfaguanidine, stated that the overall toxicity was 1 to 2 per cent and concluded that the untoward effects seem slightly more frequent with this drug than with succinylsulfathiazole.

In view of the foregoing reports it was decided to assess the value of sulfaguanidine in the treatment of bacillary dysentery, with utilization of the smaller dosage as recommended by Opper and Hale.[14]

The other sulfonamide chosen was succinylsulfathiazole. This was selected in view of the reported infrequency of toxic effects.[19]

5. Marshall, E. K., Jr.; Bratton, A. C.; Edwards, Lydia B., and Walker, Ethel: Sulfanilylguanidine in Treatment of Acute Bacillary Dysentery in Children, Bull. Johns Hopkins Hosp. **68:** 94 (Jan.) 1941.
6. Fairley, N. H., and Boyd, J. S. K.: Sulfaguanidine in Bacillary Dysentery, Lancet **1:** 20-21 (Jan. 3) 1942. Cornell, V. H.; Watt, J., and Dammin, G. J.: Sulfaguanidine in the Control of Shigella Paradysenteriae Infections in Troops, Mil. Surgeon **92:** 253 (March) 1943.
7. Poth, E. J., and Knotts, F. L.: Clinical Use of Succinylsulfathiazole, Arch. Surgery **44:** 208-222 (Feb.) 1942.
8. Hoagland, Robert J.; Harris, F. H., and Raile, R. B.: Treatment of Bacillary Dysentery Carriers, War Med. **4:** 400-403 (Oct.) 1943.
9. Smyth, C. J.; Finkelstein, M. B.; Gould, S. E.; Koppa, T. M., and Leeder, F. S.: Acute Bacillary Dysentery: Treatment with Sulfaguanidine and Succinylsulfathiazole, J. A. M. A. **121:** 1325-1330 (April 24) 1943.
10. Paulley, J. W.: Treatment of Bacillary Dysentery in the Middle East, Lancet **2:** 592 (Nov. 21) 1942.
11. Yannet, H.; Leibovitz, A., and Deutsch, J. V.: Sulfathiazole in Epidemic Sonne Dysentery, J. A. M. A. **120:** 184-188 (Sept. 19) 1942.
12. Page, S. G.: Sulfaguanidine in the Treatment of Bacillary Dysentery, Bull. U. S. Army M. Dept., January 1944, pp. 50-62.
13. Eisenoff, H. M., and Goldstein, Hyman: The Control of an Outbreak of Bacillary Dysentery with Sulfonamides, J. A. M. A. **123:** 624-626 (Nov. 6) 1943.
14. Opper, L., and Hale, V.: Sulfaguanidine in the Treatment of Dysentery (Bacterium Flexneri) Carriers, J. A. M. A. **119:** 1489-1491 (Aug. 29) 1942.
15. Cole, S. L.: Sulfaguanidine Toxicity in a Case of Ulcerative Colitis, J. A. M. A. **120:** 196-197 (Sept. 19) 1942.
16. Whyte, J. H. S.: Sulfaguanidine and Renal Damage, Brit. M. J. **1:** 373 (March 11) 1944.
17. Bunting, J. J., and Levan, N. E.: Toxic Reactions of Sulfaguanidine Therapy, J. A. M. A. **125:** 773-774 (July 15) 1944.
18. Schnitker, M. A.: Oxford Medicine, edited by Henry Christian, New York, Oxford University Press, vol. 4, part 3, p. 938.
19. Crohn, B. B.: The Clinical Use of Succinylsulfathiazole (Sulfasuxidine), Gastroenterology **1:** 140-146 (Feb.) 1943. Streicher, M. H.: Sulfonamides: A Clinical Evaluation in Infectious Diseases of the Colon, M. Clin. North America **27:** 189 (Jan.) 1943. Poth and Knotts,[7] Schnitker.[18]

Criticism might be directed to the fact that the sulfonamides producing a high blood concentration were not considered. We are fully aware that acute bacillary dysentery is not a condition confined to the intestinal mucosa but a tissue and systemic disease. Thus during the acute diarrhea phase it is probable that sulfonamides producing immediate high blood levels are desirable. However, as previously mentioned, most of the patients in this study were over the acute stage in such a short time that the problem resolved itself chiefly into eradication of the carrier state. In this situation sulfonamides producing a low blood level and a high bowel concentration might be the drugs of choice.

TABLE 1.—*Results in 181 Cases*

	Types of Therapy	No. of Cases	Results: Cures: No. of Cases	Results: Cures: Per Cent	Results: Failures: No. of Cases	Results: Failures: Per Cent
1	Controls	33	26	79	7	21
2	Sulfaguanidine (1 Gm. q. i. d. 7 days)	21	16	76	5	24
3	Sulfaguanidine (2 Gm. q. i. d. 7 days)	7	6	85.9	1	14.19
4	Succinylsulfathiazole 0.25 Gm./Kg. body weight per day for 7 days	71	70	98.5	1	1.5
5	Polyvalent bacteriophage 2 capsules (50 mg. each) q. i. d. for 2 days	49	40	81.7	9	18.3
	Total number of cases	181	158	87.3	23	12.7

As failures have been reported with all the aforementioned chemotherapeutic agents, it was only appropriate to investigate the status of the bacteriophage as a means of overcoming the carrier state. The theory of its use in the treatment of bacillary dysentery is not new. As long ago as World War I d'Herelle [20] attempted the treatment of bacillary dysentery with this specific agent, with questionable results. More recently Gantenberg,[21] in an epidemic of bacillary dysentery following the German invasion of Poland, reported inconclusive and unsatisfactory results with a polyvalent bacteriophage made by Behring. On the other hand, Compton [22] has recommended it in Cairo, where it is said to have become quite popular.

PLAN TO STUDY

In the beginning the original intention was to divide all of the cases into four equal groups, but as the epidemic assumed greater proportions it became imperative that more cases be given the type of therapy which had shown the greatest degree of success. These four groups were treated in the following manner:

1. Controls, treated symptomatically.
2. Sulfaguanidine 1 Gm. four times daily for seven days, total dose 29 Gm.
3. Succinylsulfathiazole 0.25 Gm. per kilogram of body weight daily for seven days; average total dosage 130 Gm.
4. Polyvalent dysentery bacteriophage two capsules four times daily for two days, each capsule containing 50 mg.

The last named material was supplied through the courtesy of Larkum [23] of the Army Medical School. This bacteriophage was active against the entire Shigella genus and was lyophilized so that each 50 mg. was equivalent to 25 cc. of the original phage.

Although many other patients with diarrhea were admitted to the hospital during this outbreak, only those were treated who were proved by culture to have Bacterium sonnei infection. Table 1 reveals the results obtained in 181 proved cases with the different types of therapy. It will be noted that the table includes an additional group. The creation of this group was due to a relatively high percentage of failures when the smaller dosage schedule of sulfaguanidine was used. The dosage of sulfaguanidine was doubled in this new group, 2 Gm. being given four times daily for a seven day period.

TABLE 2.—*Treatment of Failures*

	Unsuccessful Primary Therapy	Number of Failures	Successful Secondary Therapy: Control Management Alone	Sulfaguanidine, 1 Gm. q. i. d.	Sulfaguanidine, 2 Gm. q. i. d.	Succinylsulfathiazole, 0.25 Gm./Kg. B. W./Day	Polyvalent Bacteriophage, 2 Capsules q. i. d.	Succinylsulfathiazole and Bacteriophage
1	Controls, symptomatic treatment	7	0	0	0	2	5	0
2	Sulfaguanidine, 1 Gm. q. i. d. 7 days	5	0	0	0	0	3	2
3	Sulfaguanidine, 2 Gm. q. i. d. 7 days	1	0	0	0	1	0	0
4	Succinylsulfathiazole, 0.25 Gm./Kg. daily 7 days	1	0	0	0	0	1	0
5	Polyvalent bacteriophage, 2 capsules q. i. d. 2 days	9	1	0	0	1	3	4
	Total	23	1	0	0	4	12	6

In order to make this tabulation completely understandable, the criteria of cure and the determination of failure must be stated. Cultures were taken three days after the cessation of treatment in all groups except the controls. In the latter the stools were cultured for the first time after the diagnostic culture, nine days after admission. Following this initial culture, successive cultures were taken on the fifth day, twelfth day and nineteenth day following cessation of therapy. If the first or any of the succeeding cultures remained positive for the organism, the case was considered a treatment failure and secondary treatment immediately instituted.

From table 1 it is clear that the greatest percentage of cures was obtained with succinylsulfathiazole, while with the smaller dosage schedule of sulfaguanidine and the prescribed dose of bacteriophage the percentage of cures was actually no better than in those cases in which only a symptomatic regimen was given. It should be noted, however, that when the dosage of sulfaguanidine was doubled the percentage of cures showed a small but definite increase.

It is also apparent from table 1 that some failures occurred with all types of therapy, so that secondary treatment was necessary.

20. d'Herelle, F.: Bacteriophage and Its Behavior, Baltimore, Williams and Wilkins Company, 1926.
21. Gantenberg, cited by Stitt, E. R., and Strong, R. P.: Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 6, Philadelphia, Blakiston Company, vol. 1, pp. 554-556, 578.
22. Compton, Arthur: Treatment of Bacillary Dysentery, Brit. M. J. 2: 280 (Aug. 23) 1941.
23. Larkum, N. W.: Personal communication to the authors.

Table 2 demonstrates the type of therapy that was successful after the primary treatment had failed.

There were no failures after a second course of therapy with the twenty-one day period of follow-up cultures. We are fully cognizant of the fact that some of these cases might have reverted to a positive carrier state some weeks or months later. However, in a basic training center where the men are assigned for only a limited period of time, further observation of cultures beyond the twenty-one day period was not feasible. From table 2 it seems likely that a combination of a sulfonamide with a potent bacteriophage may offer some promise of success in overcoming the obstinate carrier problem.

Blood levels were obtained at the beginning and end of the treatment in the majority of patients receiving either one of the sulfonamides. With sulfaguanidine in the low dosage group, the blood levels ranged from 0.9 to 2.0 mg. per hundred cubic centimeters, with an average of 1.2 mg. per hundred cubic centimeters. It is clear that even with very small doses this drug attained a comparatively high blood concentration. On the other hand, with succinylsulfathiazole, when used in doses roughly four times the amount of sulfaguanidine, the blood showed only concentrations varying from 0.12 to 0.31 mg. per hundred cubic centimeters for an average of 0.22 mg. per hundred cubic centimeters. However, despite the wide variance in the range of blood levels, when the two sulfonamides were used there were no toxic reactions in either group. The only untoward reaction noticed was in a few patients on succinylsulfathiazole therapy, who complained of slight frequency and burning on urination.

CONCLUSION

1. One hundred and eighty-one cases of dysentery due to Bacterium sonnei were studied.

2. Low dosage treatment (4 to 8 Gm. per day for seven days) with sulfaguanidine was ineffective in eliminating carriers. No comparison relative to the effectiveness of the two sulfonamides can be made, owing to the gross disparity in dosage used.

3. Succinylsulfathiazole 0.25 Gm. per kilogram daily for seven days was efficacious in the eradication of the carrier state.

4. Polyvalent dysentery bacteriophage was no more effective than symptomatic management in rendering the patient dysentery free.

Beginning of Modern Dentistry.—The professional life of the "father of modern dentistry," Pierre Fauchard, began in the reign of the Sun King of France, Louis XIV, at whose gilt edge, resplendent court good looks—which might be marred by bad teeth—often carried off the fairest favors. Fauchard himself, graceful, elegant, courteous, might have passed for an idle nobleman. Actually he worked hard, first at Angers and later (after 1719) in Paris, at pulling, filling and reconstructing teeth and studying dental disease. Almost single handed he established dentistry as a respectable profession; before him it had been left to itinerant tinkers, vagabonds and boorish charlatans who made "tooth drawing" a laughable public spectacle. Fauchard had been trained as a naval surgeon; hence he chose the title "The Surgeon-Dentist" ("Le Chirurgien-Dentiste") for his great two volume textbook, published at Paris in 1728. Among the "aphorisms of dentistry" here selected and arranged from this first dental textbook none bears repetition today more forcibly than that one relating to the cleansing of the teeth.—The Autobiography of Science, edited by Forest Ray Moulton and Justus J. Schifferes, New York, Doubleday, Doran & Co., Inc., 1945.

DYE POISONING IN THE NURSERY

A REVIEW OF SEVENTEEN CASES

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Instances of acute poisoning by aniline and its derivatives occur not infrequently. Many of the cases reported among industrial workers and particularly in children could have been prevented had the possibility of this condition been kept in mind. It is also true that the recognition of this dye intoxication would not be so indefinite and always forthcoming if workers would be constantly on the alert in places where it is apt to occur. Therefore it is our purpose in this paper to reemphasize and warn all those concerned that this condition should never be underestimated and that today negligence of some sort is usually its chief source.

HISTORY

There have been many interesting reports on the toxic effects of aniline, its derivatives and coal tar, their mother substance. The first series of cases due to aniline-stamped diapers was in 1886. Rayner [1] reported 17 cases which appeared in London at this time. The cause of the cyanosis which appeared in these babies was an unsolved riddle among London doctors for many months. In 1929 Zeligs [2] reported 4 cases of aniline and nitrobenzine poisoning in infants. All recovered. It was found that 3 of these cases were due to skin absorption of dye from freshly stamped pads and 1 was caused by inhalation of vapors used in bedbug exterminating. He stated that articles were rendered harmless by boiling after dyeing or freshly stamping them.

Two years later Weinberg [3] described 13 cases, the poisoning resulting from the baby's body having been wrapped in clothing freshly marked with hospital identification lettering. In practically all of the cases the printing was found to be in contact with some part of the infant's body. Definite staining was found in 8 of 13 cases. The subsequent course of these children showed that all were fully recovered in from twenty-four to seventy-two hours without any observable harmful effects.

Neuland [4] reported 3 similar cases in which poisoning occurred in the same manner and Ewer [5] saw 5 infants with aniline intoxication. Two of the latter group had extensive furunculosis and therefore absorbed more of the dye. All of this last group recovered.

From the Department of Pediatrics, Touro Infirmary.

The members of the staff of Touro Infirmary gave permission to use their cases in the compilation of this report.

1. Rayner, W.: Cyanosis in Newly Born Children Caused by Aniline Marking Ink, Brit. M. J. **1**: 204 (Feb. 13) 1886.
2. Zeligs, M.: Aniline and Nitrobenzene Poisoning in Infants, Arch. Pediat. **46**: 502 (Aug.) 1929.
3. Weinberg, A. A.: Aniline Poisoning in Newborn: Thirteen Cases, Am. J. Obst. & Gynec. **21**: 104 (Jan.) 1931.
4. Neuland, W.: Poisoning of Infants and Children by Methemoglobin Producing Substances, Med. Klin. **17**: 906 (July 25) 1921.
5. Ewer, H.: Outbreak of Nitrobenzol Poisoning in Infants, Deutsche med. Wchnschr. **46**: 1078 (Sept. 23) 1920.

CHEMISTRY

Aniline has the chemical formula $C_6H_5NH_2$ and is aminobenzine. It is a colorless, oily liquid with no medicinal use. When aniline intoxication occurs in the body methemoglobinemia develops. This condition of the blood is probably the chief cause of the presenting symptoms and is due to paraminophenol and hydroxyphenylhydroxylamine,[6] which are intermediate oxidation products of aniline in the body. When the methemoglobin forms there is a short reversible reaction, with some of it being changed back into hemoglobin. Methemoglobin is a true oxide of heme and native globulin. Oxygen cannot be removed from this combination except by chemicals: methemoglobin is not capable of acting as a respiratory pigment, and a functional anemia results because of the diminution of hemoglobin available for oxygen transport.

SYMPTOMS

When there is 5 Gm. of reduced hemoglobin, cyanosis in the skin and mucous membranes appears. Some authors[7] believe that the grayish blue cyanosis which occurs with aniline intoxication is a specific symptom. They maintain that it is due to the deposition of a specially formed pigment in the subcutaneous tissues. This is borne out for them by the fact that in spite of the cyanosis the respiration remains rhythmic. This is not true when cyanosis is caused by cardiac decompensation or pulmonary involvement. Nevertheless, cyanosis depends to a large extent on the amount of methemoglobin in the body. This condition, which turns the skin slate colored, is one of the most striking of all symptoms encountered with the intoxications.

Aside from the alarming and acute symptoms concerned primarily with the companionable linkage of the blood hemoglobin and respiratory physiology, other symptoms often draw one's attention. These are evident in the nervous symptoms such as convulsions, tremor, vertigo, tinnitus and later paralysis. Dulstin[7] explains these and other nervous symptoms by saying that aniline has a direct and toxic effect on the central nervous system. He maintains that the great abundance of lipoids in the nervous tissues probably aids in the solubility of unchanged aniline found in the blood stream. Of course, many of these symptoms and signs are not detectable in the newborn for obvious reasons.

Often one sees prominent cardiac disorders having to do with disturbances in the conducting mechanism of the heart. In a group of animal experiments, Young and his associates[8] found that aniline had a direct toxic effect on the heart muscle. Proper amounts of the dye produced heart blocks and all varieties of arrhythmias. Young maintains that in acute aniline poisoning death is usually cardiac. In this series, as will be shown later, death was not due to cardiac disorder.

REVIEW OF CASES

On Jan. 5, 1944 at the Touro Infirmary a near tragedy was seen in the nursery, which was occupied by 32 babies. Seventeen of the babies unexpectedly and gradually became cyanotic and began to breathe with extreme difficulty. The diagnosis of this extensive and bizarre finding was finally made by Dr. Julian Graubarth, who remembered such a condition to have occurred in Cincinnati in 1929. The cause of these sudden symptoms was finally traced to a particular set of diapers which were stamped with ink containing aniline dye. These were accidentally sent to the nursery without first having been laundered or sterilized. The infants then absorbed the aniline through the skin of their buttocks.

At this time it would probably be wise to point out a few of the trying situations that hospitals and particularly nurseries have found themselves confronted with during the present war. There has been a shortage of diapers both in hospitals and in civilian life; therefore it can easily be seen how a nursery can exhaust its ready supply and then hastily seek what diapers it has left if the necessity becomes acute. Too, hospitals have experienced a frequent turnover in employees. This has resulted in the constant necessity of training new workers as well as combating serious problems that arise owing to lack of experience and breaks in hospital technics. Innumerable obstacles, as those that have been mentioned, have arisen in hospitals as they have in industry. It is not unlikely that situations which present themselves in the future will act as precipitating or predisposing factors to similar outbreaks.

At the time of the mishap at Touro there were 32 babies in the nursery, although only 17 developed evident aniline intoxication. All of those affected wore the unwashed diapers stamped with the dye, while the remaining 15 were wearing old diapers. A review of case histories of those children developing aniline dye poisoning revealed the following findings: One of the first things to be noted was varying degrees of anorexia in some, while others showed no disinclination to feed. All the babies showed signs of cyanosis, but this was most evident in 9 cases and lasted, on an average, ten to fourteen hours. Respiration was accelerated in every instance, but it was difficult in only 5 babies. Irritability, vomiting and loose stools were each noted in 3 cases. Other findings were hematuria (2), distention (2), jaundice (1) and an enlarged spleen (1). It was noted among most of the infants that the cry was reduced in intensity, and only 1 case showed what was thought to be a mild convulsive seizure. After ten months there have been no reports of cerebral damage. There are no reports on a refractory anemia which often follows this type of intoxication.

One infant, L. W., had serial blood pictures which revealed the following: On January 9, four days after the onset of the poisoning, the blood determinations revealed a red blood cell count of 2,500,000 and a hemoglobin of 4.9 Gm. One month later the red blood cells had risen to 3,000,000 per cubic millimeter and the hemoglobin to 9.7 Gm. The last determination was on June 9, 1944, at which time the red blood cell count was 4,300,000 and the hemoglobin was 11.6 Gm. These figures show that at the end of six months there was a complete return to normal of the red blood cell count and the hemoglobin. This picture was typical of many of the other infants.

Unfortunately, the final analysis showed that of the 17 babies involved 4 failed to survive. It is interesting

6. Goodman, L., and Gilman, A.: The Pharmacological Basis of Aniline Therapeutics, New York, Macmillan Company, 1941, p. 247.
7. Dulstin, M. S., and others: The Clinical Symptoms of Acute and Paranitroaniline Intoxications, Klin. Med. **11**: 397, 1933.
8. Young, A. G.; Muehlberger, C. W., and Meek, W. J.: Toxicological Studies of Acute Aniline Poisoning; Experimental Studies of Acute Aniline Poisoning, J. Pharmacol. & Exper. Therap. **27**: 101 (March) 1926.

to note that of the 4 deaths 3 were of premature infants, 2 of these being twins. The premature twins died of bronchopneumonia approximately three weeks later. The pathologists reported that the cause of death in the third premature child was from an intracranial hemorrhage complicated by bronchopneumonia. The fourth fatality was due to a generalized peritonitis caused by the Friedländer bacillus. In this infant no other pathologic change could be found, except for a diffuse reddening on both thighs which appeared to be a diaper rash, although an extensive search was made.

For the sake of brevity, 1 typical case will be described in detail, since many of the cases were similar in signs and symptoms:

Baby M., born several days previously, of an uncomplicated delivery, weighed 7 pounds 4 ounces (3,290 Gm.). This infant became dusky during the morning of Jan. 5, 1944. Its condition gradually became worse and respiration more difficult; therefore oxygen and 5 per cent carbon dioxide was started early in the afternoon. At this time the temperature was 99.0 F. By 5 p. m. of the same day no improvement was noticed and it was decided to administer 2 mm. of nikethamide. There was no reaction to this drug and the color became progressively worse, now being a grayish blue. At 9:30 p. m. methylene blue ½ grain, 0.032 Gm. (5 cc.), was given intravenously as well as a transfusion of 60 cc. of whole blood. Oxygen was administered until 8 o'clock the following morning. During the first day the baby was fed at 2 and 10 p. m. 1½ ounces of the nursery's routine formula.

On January 6 methylene blue was again given in the same dosage at 12, 3, 6, 9, 12, 3. Later the patient's color improved and became slightly pink. It nursed well but two clyses, each 50 cc. of 5 per cent glucose in isotonic solution of sodium chloride, were given at 10 a. m. and 4 p. m. The infant continued to improve and was discharged from the hospital five days later weighing 7 pounds 7½ ounces (3,390 Gm.). On leaving the hospital the baby still showed a faint grayish tinting of the skin.

By stating that this case was a typical one, we do not intend to imply that the therapy was the same for each of the remaining 16 babies. It must be borne in mind that the infants were treated by their individual doctors as they saw fit, but a more or less general plan was followed.

DIFFERENTIAL DIAGNOSIS

Because of the rarity of aniline dye intoxication in nurseries the diagnosis is seldom thought of when extremely pronounced and unexpected cyanosis appears. Cyanosis in the newborn or young baby may often bring to mind various congenital heart malformations. Many men have associated enlargement of the thymus gland with cyanosis. Two of the commonest causes of cyanosis to be encountered in the infant are pneumonia and aspiration. Aspiration of a foreign body could be milk curds, mucus, mechanical objects and the like. Intracranial hemorrhage, common poisons such as sulfonamides, nitrites or ferrous cyanide, allergies from insect sprays or disinfectants and the escaping of illuminating gas often are first noticed because of the peculiar grayish blue tint that occurs as one of their early symptoms.

In this series of cases food was considered as the causative agent for only a short time in the beginning. It was found that all of the babies, whether breast fed or artificially fed, were affected similarly by the then unknown cause. Even babies who were brought directly from the delivery room and who received nothing by mouth developed the condition within a short time.

TREATMENT

In the Touro incident treatment centered around the use of methylene blue, oxygen and 5 per cent carbon dioxide and whole blood transfusions. Of the total number, 17, 12 infants were given methylene blue in the dosage of ½ grain (5 cc.) in each of their feedings for two days. All were fed by a three hour schedule. This left 3 babies that did not receive the methylene blue. The oxygen and 5 per cent carbon dioxide was given to 6 and blood transfusions to 9. Each of the 4 babies that died, except the premature twins, was given the same treatment. Transfusion was found to be too difficult a procedure on them.

Methylene blue and oxygen had no apparent effect on the time or type of recovery of any of the infants. Just as complete and just as speedy a recovery was seen in the 3 infants who had no treatment other than change of diapers, isolation and transfusion. Even in 2 of the infants who received no therapy whatever recovery was similar and uneventful. Had the diagnosis been apparent at the time, no treatment other than transfusion would have been tried. It has never been proved whether methylene blue has any effect on accelerating the rate of reduction of methemoglobin to hemoglobin, and in high concentration it converts the ferrous iron of reduced hemoglobin to reduced iron, thus producing methemoglobin. The use of oxygen in treating cyanosis of this type is not rational, since the methemoglobin reduces the amount of hemoglobin that can act as a respiratory pigment.

It is needless to say that the treatment lies first in the prevention, then in removing the source, transfusions with whole blood or red cells suspended in saline solution, giving plenty of fresh air and, finally, isolation. In a very profound case of cyanosis due to aniline, transfusions of whole blood or red cells suspended in saline solution would be the most logical therapeutic agent to use.

CONCLUSION

1. In 17 cases of aniline dye poisoning in a nursery the intoxication was caused by diapers stamped with ink containing aniline dye. Thirteen babies recovered; 4 died from unrelated causes.

2. The prevention of this type of poisoning rests in the adherence of a strict aseptic technic in handling all supplies entering the nursery. If this is done an ink-containing aniline dye could be used, as it becomes innocuous after the first laundering.

3. It must be remembered that only small proportions of aniline dye are necessary to produce intoxication in infants. This is true also for adults.

4. Treatment consisted primarily in removing the source of intoxication, oxygen and 5 per cent carbon dioxide, transfusion, methylene blue and isolation. Methylene blue and oxygen therapy were found to be unnecessary, and transfusions are not imperative unless the condition is acute and severe.

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THE USE OF HUMAN IMMUNE SERUM GLOBULIN (GAMMA GLOBULIN)

IN INFECTIOUS (EPIDEMIC) HEPATITIS IN THE MEDITERRANEAN THEATER OF OPERATIONS

II. STUDIES ON TREATMENT IN AN EPIDEMIC OF INFECTIOUS HEPATITIS

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Because of the long period of convalescence following infectious hepatitis with resulting loss of manpower to the United States Army, the present study was conducted in suitable groups in the Mediterranean Theater of Operations in order to determine whether or not gamma globulin is an effective therapeutic agent in lessening the severity of the disease and in shortening the period of convalescence. Stokes and Neefe,[1] pointing out that globulin is often of value if injected soon after the onset of the initial symptoms of measles,[2] suggested its trial as a therapeutic measure in early infectious hepatitis.

Through the cooperation of an air force in this theater, patients developing infectious hepatitis were made available for the study. The majority of the patients came from one bombardment group and were diagnosed by the squadron physicians, who had extensive experience with the disease. Patients were chosen for the study as soon as possible after the onset of symptoms and signs suggestive of early, preicteric infectious hepatitis. Typical symptoms consisted of an acute onset of fever, chilliness or chills, headache, nausea, vomiting, anorexia and abdominal pain. Suggestive signs consisted of right upper quadrant tenderness and spasm, often with a palpable and tender liver. If there was any suggestion of scleral icterus, the patient was not included in the series. Alternate patients arriving at each squadron or headquarters dispensary were given 0.3 cc. of gamma globulin per pound of body weight. The average total dose of globulin was 45 cc., half of which was injected into each buttock. The only reaction consisted of pain and tenderness at the site of injection owing to the distention caused by the large dose administered. The pain was much less pronounced if the globulin was injected after the patient had been hospitalized and muscular movement thus limited. However, the globulin was administered as soon as a tentative diagnosis of early, preicteric hepatitis was made. The injected and control patients were evacuated from the dispensaries as soon as possible by plane to the 26th General Hospital in order to maintain a uniform program of clinical and laboratory follow-up of the group. It was understood that, in the attempt to diagnose hepatitis so early in the course of the disease, errors would be inevitable and patients with diseases other than infectious hepatitis would be included. However, it was felt that such cases would fall equally into the injected and control groups and could subsequently be discarded.

A total of 278 patients were admitted to the study; 70 of these developed jaundice subsequent to the time of injection of globulin. The great majority of the remaining patients proved to have hepatitis without jaundice, as indicated by the liver function tests and the subsequent course of the disease.

Before reviewing the hospital course of the injected and control patients, it appeared that the following criteria might be of value in determining whether or not globulin had an attenuating effect on infectious hepatitis once the disease had started: (*a*) the incidence of jaundice occurring in the injected and control groups, (*b*) severity and duration of jaundice, (*c*) length of hospitalization, (*d*) the duration of the period in which various laboratory tests showed activity of the disease and (*e*) the frequency of relapse in the two groups.

On the basis of the foregoing criteria the following results were obtained:

(*a*) *Incidence of Jaundice in Injected and Control Patients.*—Of the 70 patients who developed jaundice subsequent to admission to the study, 31 had received globulin and 39 were control patients. The difference between the two groups is not sufficiently great to be significant.

(*b*) *Severity and Duration of Jaundice.*—The severity and duration of jaundice proved to be unsatisfactory criteria for judging the attenuating value of globulin, as their variation within each group was so great. Cases with mild and transient jaundice fell equally into the injected and control groups.

(*c*) *Length of Hospitalization.*—Subjective symptoms determined to a great degree the length of hospitalization necessary in this disease, and since these were appreciably affected by the patient's desire or unwillingness to return to his unit it was impossible to use the period of hospitalization for comparison.

(*d*) *Length of Time in Which Laboratory Tests Indicated Activity of Disease.*—The only test which was conducted daily for each of the patients and could therefore be accurately compared in the two groups was the methylene blue test.[3] The average duration of a positive methylene blue test, counting from the first day of scleral icterus, was ten days for the injected patients and 9.9 days for the controls. Since the cephalin cholesterol flocculation test and the sulfobromophthalein test were not performed at identical intervals for all patients, the time required for these to return to normal could not be accurately determined for the two groups. Therefore the methylene blue test, the only test permitting comparison of the injected and control patients, revealed no evidence in favor of an attenuating effect of globulin.

(*e*) *Frequency of Relapses.*—Four patients in the control group and 1 in the injected group developed relapse of the disease. Since the total number of

This work was carried out under the direction of the Commission on Measles and Mumps of the Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, U. S. Army.

The gamma globulin used in these studies was obtained from pools of plasma, each pool representing 3,000 to 5,000 individuals, collected by the American Red Cross and fractionated, according to the method of Cohn and his co-workers, by various biologic manufacturers. These pools were obtained originally from groups of individuals in the Eastern and Southern regions of the United States.

1. Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin, J. A. M. A. **127:** 144 (Jan. 20) 1945.

2. Stokes, J., Jr.; Maris, E. P., and Gellis, S. S.: Use of Concentrated Normal Human Serum for Prevention and Attenuation of Measles, J. Clin. Investigation **23:** 531, 1944.

3. Franke, K.: Methylenblau, ein einfaches sehr empfindliches Reagens Zum Nachweis von Bilirubin, Med. Klin. **27:** 94, 1931. Gellis, S. S., and Stokes, J., Jr.: The Methylene Blue Test in Infectious Hepatitis, J. A. M. A. **128:** 782 (July 14) 1945.

patients with relapse is so small, this difference does not appear to be significant.

It was difficult to compare the cases of hepatitis without jaundice in the treated and control groups. Variation in the severity and duration of this form of the disease was even more evident than in hepatitis with jaundice. No clearcut evidence was obtained indicating an attenuation in the treated group.

COMMENT

In accordance with observations recorded in the majority of virus diseases that homologous immune bodies rarely are effective therapeutically when the symptoms have fully developed, immune bodies also in this epidemic disease appear to have little, if any, therapeutic value. As the present data do not include a large number of cases at their earliest onset, it is still possible that larger amounts of immune bodies in the form of gamma globulin or, more properly, gamma globulin from pools of convalescent plasma may prove effective in therapy. The obvious difficulty in obtaining cases of this disease at their earliest onset is very great and renders the possibility of such a therapeutic approach highly problematic.

The additional possibility that gamma globulin may be of value in the prevention of relapses or recurrences of the disease deserves further investigation.

SUMMARY

A program designed to test the effectiveness of human immune serum globulin (gamma globulin) in the attenuation of infectious hepatitis was conducted in an air force in the Mediterranean Theater of Operations.

Gamma globulin, 0.3 cc. per pound of body weight, was administered intramuscularly to alternate patients presenting the earliest symptoms suggestive of infectious (epidemic) hepatitis.

No evidence was obtained in the patients studied in favor of an attenuating effect of gamma globulin when administered early in the course of the disease.

Clinical Notes, Suggestions and New Instruments

PENICILLIN THERAPY IN PYLEPHLEBITIS

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Pylephlebitis is an inflammation of the portal vein caused by an acute suppurative process in that part of the abdomen drained by the portal vein. The disease carries a high mortality because of the multiple embolic liver abscesses arising from the infected thrombi in the portal system.

The most common condition causing this disease is acute appendicitis; however, gangrenous cholecystitis, infected thrombotic hemorrhoids, diverticulitis or pelvic suppuration may precipitate a portal thrombosis.

The case reported here followed an acute attack of appendicitis, so I shall confine the discussion to this disease.

In 1897 Armstrong[1] reporting in England, stated that this complication caused 5 per cent of the deaths due to appendicitis. Hawkes[2] in 1938 analyzed a series of 1,463 cases of acute appendicitis in which portal thrombosis occurred but 12 times. This lowered incidence can be attributed to earlier operative intervention in acute appendicitis.

From the Surgcal Service, U. S. Marine Hospital, Chicago.

1. Armstrong, G. E.: Introduction to a Discussion on Appendicitis, Brit. M. J. **2**: 945, 1897.

2. Hawkes, S. L.: Thrombophlebitis of Appendical Vein, Surg., Gynec. & Obst. **66**: 62, 1938.

PATHOLOGY

According to Crossland[3] pylephlebitis usually follows pronounced appendical disease. Busch and Spivack[4] reported 4 fatal cases in a series of 635 cases of acute appendicitis. Two of these were gangrenous appendicitis with perforation, and 2 were appendical abscesses. This fulminating type of appendicitis is usually attributed to the streptococcus. Early in the disease a septic thrombus is found in the terminal branches of the ileocolic vein, and if the thrombus is not removed at time of operation with the appendix the thrombus extends upward or breaks off and lodges in the liver. Early in the disease positive blood culture is rare. Later, when the liver is riddled with abscesses and its venous system is thrombosed, they may be obtained. Empyema of the right chest by direct extension from the liver may occur. Jaundice due to liver destruction is a late finding. Ascites is common and is associated with the massive portal obstruction.

SYMPTOMATOLOGY

In addition to the clinical history suggesting appendicitis, the patient may have a chill. Colp[5] found a chill in 6.8 per cent of his cases and Kelly and Hurdon in 15 per cent of theirs. Temperature elevations are out of proportion to the amount of appendical disease. Severe prostration accompanies even the milder cases of thrombophlebitis of the appendical vein.

TREATMENT

Prophylaxis by early removal of the appendix when inflamed is mandatory. Probably few cases would develop if all cases should come to operation during the first twenty-four hours.

Treatment by ligation of the veins in the ileocolic angle has been most disappointing. Wilms[6] first suggested this, and his operation was modified by Braun.[7] Routine ligation of the ileocolic vein is to be condemned, but all should be inspected and ligated if thrombosed.

Sulfanilamide has been used with success in 2 cases as reported by Ottenberg and Berck.[8]

REPORT OF CASE

History.—H. H., a man aged 22, a seaman, admitted June 2, 1944, complained of dull pain in the right groin and a swollen abdomen. The patient had an operation for appendicitis, gangrenous type, done Feb. 10, 1944. This operation was done as an emergency measure at a hospital along the Florida coast. He was transferred to the Marine Hospital in Chicago on June 2, 1944. The history forwarded with the patient stated that on Feb. 10, 1944 the patient presented himself with the typical signs and symptoms of acute appendicitis and was given an immediate operation. The appendix was suppurative with exudate on its outer surface; there were local peritonitis and a turbid peritoneal fluid. Cultures were not made. During the patient's convalescence he developed drainage from the wound, but it healed after about three weeks. On the second postoperative day the patient developed chills and a septic temperature began; that is, he had an afternoon elevation with temperatures running to 101 and 102 F. and chills nearly every day. The white blood cell count was elevated to about 18,000, but the blood cultures were repeatedly negative. The patient had no particular complaints except anorexia and extreme weakness. He perspired freely and subsequently developed an anemia, which was treated with iron and blood transfusions. On April 24 he complained of shortness of breath and fulness of the abdomen; fluid was demonstrated in the right chest. This was subsequently aspirated. The first specimen was slightly turbid and in appearance was serosanguineous. Repeated aspiration a few days later revealed that the specimen was more purulent, was bile stained and had a peculiar odor which is usually associated

3. Crossland, P. M.: Pylephlebitis Complicating Appendicitis, U. S. Nav. M. Bull. **39**: 398, 1941.

4. Busch, I., and Spivack, A. H.: Observations on Acute Appendicitis, Surg., Gynec. & Obst. **70**: 241, 1940.

5. Colp, R.: Treatment of Pylephlebitis of Appendicular Origin, Surg., Gynec. & Obst. **43**: 627, 1926; Chills in Acute Appendicitis, Ann. Surg. **85**: 257, 1927.

6. Wilms: Venenunterbindung bei eitriger Pfortaderthrombose nach Appendicitis, Zentralbl. f. Chir. **36**: 1041, 1909.

7. Braun, H.: Die Unterbindung der Vena ileocolica bei mesenterialer Pyämie nach Appendizitis, Beitr. z. klin. Chir. **86**: 314, 1913.

8. Ottenberg, R., and Berck, M.: Sulfanilamide Therapy for Pylephlebitis and Liver Abscesses, J. A. M. A. **111**: 1374 (Oct. 8) 1938.

with a colon bacillus infection. At this time a diagnosis of pylephlebitis or thrombophlebitis of the portal veins, with liver abscess, was made. The patient developed a transitory jaundice, the liver became definitely enlarged and the patient became weaker. He was put on sulfanilamide therapy, 1 Gm. being given every four hours, and penicillin. A total of 10,000 units of penicillin was given before the patient was transferred to our hospital.

On admission, June 2, the patient had some pain in the abdomen and pain in his right groin. He had little appetite and felt weak. He was not taking sulfonamide drugs at this time but was on a high vitamin diet. The pain in the abdomen seemed to remain stationary in the right side but at times appeared to radiate toward the midline and down the right leg. The site of the operation did not pain him at that time. However, he felt "full in the abdomen" and was sure that he contained a lot of fluid. He had no pain in the right chest and had no dyspnea on exertion. He was slightly constipated and had to take liquid petrolatum to keep his bowels open. He had no dependent edema nor any pain or swelling in the legs which would indicate phlebitis of the femoral or iliac veins. A systemic review of his symptoms was noncontributory except for his present complaints.

His past history was noncontributory.

Physical Examination.—The patient was poorly nourished but fairly well developed and appeared acutely ill. There was evidence of great weight loss. He was too sick to weigh at this time but he stated that he had lost about 60 pounds. The eyes, ears, nose and throat were essentially normal. The ribs were prominent; the supraclavicular and infraclavicular fossae were depressed. There was limitation of excursion right and left, especially anteriorly. There was dulness to percussion in the left base, but in the right base the dulness was more evident and extended to the level of the nipple line anteriorly and to the level of the sixth rib posteriorly. There was no excursion of the diaphragm on the right. There were bronchial and vesicular breath sounds, right and left, with the breath sounds diminished in the bases. There were no rales audible. Tactile and vocal fremitus were diminished. There was tenderness over the posterior right lumbar area on Murphy's percussion. The heart was normal except for a roughened first sound. The pulse rate was 120, the blood pressure 125/80. The pulse, while rapid, was regular and of good quality. The abdomen was greatly distended and a fluid wave elicited. There was some shifting dulness but with so much fluid it was hard to demonstrate. The liver was enlarged 3 fingerbreadths below the costal margin, but it was smooth and some tenderness was present. The genitourinary examination gave essentially normal results. There were some muscle aches and pains in the extremities and in the joints on extreme ranges of motion. There was 1 plus edema over the dorsum of the feet. The temperature on admission was 38.2 C. (100.7 F.), the pulse rate 118.

Laboratory Work on Admission.—Red blood cells numbered 3,350,000, white blood cells 10,500; hemoglobin was 61.4 per cent, 9.5 Gm.; small mononuclears 22, stabs 34, neutrophils 41, 1 Türk cell, an occasional target cell. The urine was amber color and showed a trace of albumin; the specific gravity was 1.014. The Wassermann and Kahn reactions were negative; blood culture showed no growth after ten days; the icterus index was 10 units; the blood was of type O. Serum protein was 6.8 Gm. per hundred cubic centimeters of serum. Repeated blood cultures were negative. Repeated examinations of stools for parasites were negative for Endameba histolytica. X-ray examination at time of admission revealed a large liver with elevation of the right diaphragm.

Course.—The patient was observed for four days after admission and given a high protein, high vitamin diet with iron therapy. During that time he had temperature elevations that ran from 39 C. (102.2 F.) in the afternoon to 37.6 C. (99.7 F.) in the morning. On June 6 a soft area was noticed on the posterior chest wall at the level of the tenth rib, in the posterior axillary line. Under nitrous oxide anesthesia this soft mass was incised and drained. The pus was thick and green and had the appearance of concentrated streptococcus pus. The abscess cavity extended about 12 cm. in all directions and went beneath the latissimus dorsi deep to the tenth rib. We were unable to demonstrate any connection with the liver or with the subdiaphragmatic space. The pus was cultured both aerobically and anaerobically. Guinea pig inoculation for tubercle bacilli was negative; aerobic cultures were negative, but we were able to demonstrate anaerobic staphylococci on culture. Consequently the patient was placed on penicillin therapy, receiving 20,000 units intramuscularly every three hours until 2,000,000 units had been given. The patient had repeated aspirations of the abdomen while in the hospital so that we could control the amount of abdominal fluid. These aspirations were done about every five days, and approximately 1,500 cc. of ascitic fluid would be removed at each time. The patient continued to have low grade spiking temperatures, after the incisions and drainage of the abscess of the right chest wall, until June 27. At that time an aspiration of the liver was done in the posterior axillary line below the level of the twelfth rib so that we would remain retroperitoneal and outside of the pleural space. On June 27 an abscess of the liver was demonstrated; it contained about 100 cc. of thick greenish yellow purulent material and also contained much cellular débris. There was a slight putrefactive odor not characteristic of any organism. It was sent to the laboratory, and again an anaerobic staphylococcus was demonstrated. The abscess was then irrigated with saline solution and the washings were sent to the laboratory and a search made for amebas. None were demonstrable here, just as none had been demonstrable in the repeated stool examinations. Into the abscess cavity was injected 25,000 units of penicillin dissolved in distilled water. Repeated explorations were then made, but we were unable to demonstrate any more abscesses in the liver. Roentgenograms were made on several occasions after 100 cc. of air had been placed within the liver abscess; thus we were able to demonstrate that the abscess was in the liver and not in the subdiaphragmatic space.

The patient continued to improve; his anemia became less pronounced and the abscess of the liver was repeatedly aspirated. On June 30 we again opened the posterior wound in the right chest wall and demonstrated a connection between the abscess of the right posterior chest wall and the liver. Several Penrose drains were inserted deep into the chest wall and into the fistulous tract leading to the liver. This wound was also irrigated with a penicillin solution. On June 30, after we had drained the liver abscess, the patient became afebrile and continued so throughout the rest of his stay in the hospital. On July 8 lipiodol was injected into the fistulous cavity leading to the liver, and x-ray consultant Dr. J. T. Case interpreted the films as showing a large liver abscess which permitted the lipiodol to be demonstrated over a wide area, or perhaps as a liver abscess with numerous pockets in the abscess.

Recovery was very slow, owing to the fact that the patient had anemia and a severe debilitating disease. He was discharged from our hospital on September 19 as improved. He has returned as an outpatient several times since then and at present is able to return to work. He was last seen at this hospital in February 1945, at which time his weight was almost up to his normal of 190 pounds (86 Kg.). He was moving about as well as ever, felt energetic and was given a fit for duty certificate so that he could return to sea. His posterior right thoracic wound, through which the liver abscess was drained, was healed with a nontender adherent scar and he said that he had no abdominal pain, and his abdomen was not distended. At the time of discharge the red blood cell count was 4,850,000, with hemoglobin 90.4 per cent, 14.0 Gm. The white corpuscle count was 10,750, with 51 per cent neutrophils, 35 per cent stabs giving a total of 86 per cent polymorphonuclears, 12 per cent mononuclears and 2 transitional cells. There was a moderate toxic granulation of the polymorphonuclears. There was a tendency for the red cells to be of a hypochromic type. At the time of discharge the urine had a specific gravity of 1.022

and was negative for albumin, sugar, pus, casts or epithelial cells. He was advised to report for follow-up examination in six months.

SUMMARY

Pylephlebitis follows pronounced appendical disease and, while infrequent, should be considered when systemic symptoms are severe.

Thrombosis of the appendical vein may be a progressive disease, with extension into the portal vein, and result in multiple liver abscesses.

After appendicitis is diagnosed, chills, fever and prostration are the cardinal signs of this disease.

Treatment is early operation, early ligation of the thrombosed ileocolic vein. If the disease progresses in spite of this treatment, chemotherapy with sulfadiazine and penicillin should be instituted.

A case of pylephlebitis ended in complete recovery.

A MEANS OF INDUCING OLIGURESIS DURING PENICILLIN ADMINISTRATION

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In reference to the published material suggesting the advisability of urine concentration in the penicillin therapy of gonorrhea, the following suggestion is made: Pitressin to accomplish this end was suggested to me during observations on pitressin and its influence on human urine secretion. Because of the paucity of clinical material and facilities at sea the suggestion is passed on for evaluation by those more favorably situated for such study.

The antidiuretic principle of posterior pituitary was first noted by von den Velden [1] in 1913.

Gargle, Gilligan and Blumgart [2] in 1928 showed that it was the pressor function of the posterior pituitary that was responsible for the hormone's antidiuretic principle.

Leberman [3] in 1930 made use of this fact by employing the hormone to produce urinary concentration in the execution of renal concentration tests.

McQuarrie and his associates [4] in 1936 used the period of diuresis which follows prolonged antidiuresis with pituitary to relieve edema in certain instances of nephrosis.

Lich and Lewis [5] have utilized pitressin induced antidiuresis to eliminate the period of water deprivation preceding intravenous pyelography.

In studying the effect of pitressin in normal man both during increased water intake and in normal conditions it was found that antidiuresis is maintained from three to five hours following the subcutaneous administration of 0.5 cc. of pitressin. This effect may be prolonged with the repeated administration of pitressin at intervals of three hours and may be continued for a twenty-four hour period. Hence this would seem a simple positive method to affect urinary concentration if this is essential in penicillin medication for the treatment of gonococcic urethritis.

SUMMARY

The use of pitressin subcutaneously is suggested to produce oliguresis during periods of penicillin therapy. It has been suggested in the literature that urinary concentration is beneficial in penicillin therapy of gonococcic urethritis.

1. von den Velden, R.: Die Nierenwirkung von Hypophysenextrakten beim Menschen, Berl. klin. Wchnschr. **50**: 2083, 1913.
2. Gargle, S. L.; Gilligan, D. R., and Blumgart, H. L.: The Antidiuretic Effect of the Oxytocic and Pressor Principles of the Extract of the Pituitary, New England J. Med. **198**: 169, 1928.
3. Leberman, F.: Funktionelle Nierendiagnostik durch Hypophysenpräparate, Med. Welt **4**: 1144, 1930.
4. McQuarrie, I.; Thompson, W. H., and Ziegler, M. R.: Effects of Posterior Pituitary Extract on Water and Mineral Exchanges in Edema, J. Pediat. **8**: 277, 1936.
5. Lich, R., Jr., and Lewis, P. J.: The Use of the Antidiuretic Property of Pitressin in Excretory Pyelography, J. Urol., to be published.

Special Article

NEW DOSAGE FORMS OF PENICILLIN

STATEMENT CONCERNING CERTIFIABLE PENICILLIN PRODUCTS, INCLUDING RECOMMENDED INDICATIONS, DOSAGES AND PRECAUTIONS

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BOSTON

ROBERT P. HERWICK, PH.D., M.D.

WALTON VAN WINKLE JR., M.D.

AND

LAWRENCE E. PUTNAM, M.D.
U. S. Food and Drug Administration
WASHINGTON, D. C.

On July 6, 1945 the Federal Food, Drug and Cosmetic Act was amended to provide for the certification of batches of drugs composed wholly or partly of any kind of penicillin. The Federal Security Administrator, in accordance with the provisions of this amendment, has promulgated regulations providing such standards of identity, strength, quality and purity as will insure the safety and efficacy for use of a number of penicillin products. Before distribution in interstate commerce, each manufacturer must submit samples of each batch of any penicillin product to the Food and Drug Administration for examination and must obtain a certificate showing that the batch complies with the applicable regulations.

Inclusion of the penicillin products listed in the regulations providing for certification was based on a review of the available scientific evidence and on information developed in consultations with experts in the field of chemotherapy and the medical and scientific staffs of interested manufacturers. The suggestions regarding indications, dosages and precautions reflect as closely as possible the experience of experts in penicillin therapy. These suggestions are necessarily conservative, since experience with many of these products has been limited and there are many questions yet unanswered. As additional evidence accumulates it may be possible to extend the indications and alter the dosage schedules set forth in the following paragraphs.

PARENTERAL PRODUCTS

SODIUM PENICILLIN AND CALCIUM PENICILLIN

Sodium penicillin and calcium penicillin are so purified and dried that the final products have a potency of not less than 500 units per milligram. They are sterile, nontoxic and nonpyrogenic and have a moisture content of not more than 2.5 per cent. They are packaged in 100,000 unit, 200,000 unit, 500,000 unit, 1,000,000 unit and 5,000,000 unit sizes.

Indications and Dosage.—

GROUP I INDICATIONS

1. All staphylococcic infections with and without bacteremia:
   Acute and chronic osteomyelitis.
   Carbuncles—soft tissue abscesses.
   Meningitis.
   Cavernous or lateral sinus thrombosis.
   Pneumonia—empyema.
   Carbuncle of kidney.
   Wound infections—burns.
   Endocarditis.

2. All cases of clostridia infections:
   Gas gangrene.
   Malignant edema.
3. All hemolytic streptococcic infections with bacteremia and all serious local infections:
   Cellulitis.
   Mastoiditis with intracranial complications, i. e. meningitis, sinus thrombosis and so on.
   Pneumonia and empyema.
   Puerperal sepsis.
   Peritonitis.
   Endocarditis.
4. All anaerobic streptococcic infections:
   Puerperal sepsis.
   Localized infections elsewhere.
5. All pneumococcic infections of:
   Meninges.
   Pleura.
   Endocardium.
   All cases of sulfonamide-resistant pneumococcic pneumonia.
6. All gonococcic infections.
7. All cases of anthrax.
8. All cases of chronic pulmonary suppuration in which surgical treatment is contemplated.
9. All meningococcic infections failing to respond to sulfonamides.
10. All cases of bacterial endocarditis due to susceptible organisms.
11. Erysipeloid (swine erysipelas).
12. Vincent's infection.
13. Prophylactic use in prevention of possible secondary infection following tonsillectomy and tooth extraction in cases with a history of rheumatic fever or in rheumatic heart disease, in congenital heart disease and in other conditions in which secondary infection may occur (infected teeth; tonsils).

GROUP II INDICATIONS

Penicillin has also been found to be an effective agent in the following diseases, but its position has not been definitely defined and will require additional experimental work:

1. Syphilis.
2. Actinomycosis.
3. Diphtheria, in conjunction with antitoxin.

GROUP III CONDITIONS OF QUESTIONABLE VALUE

Penicillin is of questionable value in mixed infections in which the predominating organism is of the gram negative flora—i. e.:

1. Ruptured appendix with peritonitis.
2. Liver abscesses.
3. Urinary tract infections due to Escherichia coli.
4. It is also of questionable value in rat bite fever due to Streptobacillus moniliformis.

GROUP IV CONDITIONS IN WHICH PENICILLIN IS INEFFECTIVE

1. All gram negative bacillary infections:
   Typhoid—paratyphoid.
   Dysentery.
   Escherichia coli.
   Hemophilus influenzae.
   Bacillus proteus.
   Bacillus pyocyaneus.
   Brucella melitensis (undulant fever).
   Pasteurella tularensis (tularemia).
   Friedländer's bacillus.
2. Tuberculosis.
3. Toxoplasmosis.
4. Histoplasmosis.
5. Acute rheumatic fever.
6. Lupus erythematosis, diffuse.
7. Infectious monunucleosis.
8. Pemphigus.
9. Hodgkin's disease.
10. Acute and chronic leukemia.
11. Ulcerative colitis.
12. Coccidioidomycosis.
13. Malaria.
14. Poliomyelitis.
15. Blastomycosis.
16. Nonspecific iritis and uveitis.
17. Moniliasis.
18. Virus infections.
19. Cancer.

Method of Preparing Penicillin for Treatment.—As penicillin is extremely soluble, it may be dissolved in small amounts of sterile distilled, pyrogen-free water, in sterile isotonic solution of sodium chloride or in sterile 5 per cent dextrose solution. When large unit sizes are being used in hospitals, the contents of the ampule should be dissolved in water or saline solution so that the final concentration is 5,000 to 50,000 units per cubic centimeter, depending on the circumstances of the case. This solution should be stored under aseptic precautions in the ice box and made up freshly every day. Solutions for local or parenteral use may be diluted further, depending on the concentration desired.

A. For intravenous injection:

1. The dry powder may be dissolved in sterile isotonic solution of sodium chloride in concentrations of 10,000 to 50,000 units per cubic centimeter for direct injection through a syringe.
2. The dry powder may be dissolved in sterile saline solution or 5 per cent glucose solution in lower dilution (25 to 50 units per cubic centimeter) for constant intravenous therapy.

B. For intramuscular injection:

1. The total volume of individual injections should be small, i. e. 10,000 to 50,000 units per cubic centimeter of isotonic solution of sodium chloride. It may also be given by constant intramuscular drip, 120,000 units in 250 cc.

Methods of Administration of Penicillin.—There are three common methods of administering penicillin—intravenous, intramuscular and topical. Subcutaneous injections are likely to be painful and should be avoided. The route of choice is intramuscular.

Dosage.—The dosage of penicillin will vary from one patient to another depending on the type and severity of infection. The objective in every case is to bring the infection under control as quickly as possible. In most cases a minimum of 100,000 units daily will be required.

It is well to remember that penicillin is excreted rapidly in the urine so that following a single injection it is often impossible to detect it in the blood for a period longer than two to four hours. It is well, therefore, to use repeated intramuscular or intravenous injections every three or four hours or to administer it as a continuous infusion.

A. In serious infections with or without bacteremia an initial dose of 15,000 or 20,000 Oxford units with continuing dosage as:

1. Constant intravenous injection of isotonic solution of sodium chloride containing penicillin so that 5,000 to 10,000 Oxford units is delivered every hour, making a total of 120,000 to 240,000 units in a twenty-four hour period. One half the total daily dose may be dissolved in a liter of isotonic solution of sodium chloride and allowed to drip at the rate of 30 to 40 drops per minute.
2. If a continuous intravenous drip is undesirable, 20,000 to 40,000 units may be injected intramuscularly every three or four hours.
3. After the temperature has returned to normal, the penicillin may be continued as long as there are any signs of active infection.

B. In chronically infected compound injuries, osteomyelitis and the like the dosage schedule should be 20,000 units every two hours or 40,000 units every four hours parenterally with local treatment as indicated. This dosage schedule may have to be increased, depending on the seriousness of the infection and the response to treatment. The best results are obtained in these cases when penicillin is combined with adequate surgical treatment.

C. Gonorrhea:

1. Twenty-five thousand units every three hours intramuscularly for five doses. The results of treatment should be controlled by culture of exudate. All patients failing to respond to the first course should be retreated.

D. Empyema:

1. Penicillin in isotonic solution of sodium chloride should be injected directly into the empyema cavity after aspiration of pus or fluid. This should be done once or twice daily, using 50,000 or 100,000 units, depending on the size of the cavity, type of infection and number of organisms. Penicillin solution should not be used for irrigation.

E. Meningitis:

1. Penicillin does not penetrate the subarachnoid space in appreciable amounts, so that it is necessary to inject penicillin into the subarachnoid space or intracisternally in order to produce the desired effect. Ten thousand units diluted in isotonic solution of sodium chloride in a concentration of 1,000 units per cubic centimeter should be injected once or twice daily, depending on the clinical course and the presence of organisms.

F. Bacterial Endocarditis:

1. Penicillin is the best agent available for the treatment of bacterial endocarditis. Penicillin alone is as effective as penicillin combined with heparin. The treatment should be continued for three weeks or longer, depending on the individual case. The intramuscular route is the one of choice, although in a few instances it may be desirable to use the continuous intravenous route in order to obtain the maximum effect. The dosage should range from 200,000 to 300,000 units a day if the best results are to be obtained.

PENICILLIN WITH DILUENT

Penicillin with diluent is a combination package of penicillin and a suitable solvent such as water for injection, 5 per cent dextrose injection or isotonic solution of sodium chloride.

Indications and Dosage.—Same as for sodium penicillin and calcium penicillin.

PENICILLIN IN OIL AND WAX

Penicillin in oil and wax is a suspension of calcium penicillin in a menstruum of refined peanut oil in which white wax is dispersed. It is packaged in 100,000 units per cubic centimeter, 200,000 units per cubic centimeter and 300,000 units per cubic centimeter concentration. The white wax content of the 100,000 units per cubic centimeter and 200,000 units per cubic centimeter concentrations is not less than 3 per cent and of the 300,000 units per cubic centimeter concentration not less than 4.7 nor more than 4.9 per cent. The calcium penicillin used in the 300,000 unit per cubic centimeter concentration has a potency of not less than 900 units per milligram, and that in the other concentrations has a potency of not less than 750 units per milligram.

Indications and Dosage.—Gonorrhea, acute staphylococcic and streptococcic infections and pneumonia.

All conditions require a minimum of 300,000 units per day. Preparations containing 200,000 units per cubic centimeter may be administered at twelve hour intervals. If the quantity is 100,000 units per cubic centimeter, administration at eight hour intervals is necessary. Rotation of the site of injection is desirable; the upper outer quadrants of the buttocks, the anterior thighs and triceps are suggested sites.

Gonorrhea.—Three hundred thousand units as a single injection or 200,000 units as an initial injection followed by 100,000 units in twelve hours, or three injections at eight hour intervals of 100,000 units each. In the presence of complications such as arthritis, endocarditis and epididymitis the dosage should be intensified and prolonged.

Pneumonia and Acute Staphylococcic and Streptococcic Infections.—A minimum of 300,000 units daily, preferably in divided doses and continued until the temperature returns to normal and other evidence of infection disappears.

Precautions.—DO NOT USE INTRAVENOUSLY. Do not use in those conditions listed in groups III and IV under "Sodium Penicillin" and "Calcium Penicillin."

ORAL PRODUCTS

TABLETS BUFFERED PENICILLIN, CAPSULES BUFFERED PENICILLIN

Tablets buffered penicillin and capsules buffered penicillin contain one or more of the buffer substances sodium citrate, citric acid, aluminum hydroxide, calcium carbonate, magnesium oxide and aluminum-dihydroxy-amino acetate. The potency of each tablet or capsule is not less than 20,000 units, and the number of tablets or capsules in each single package is such that the total number of units therein is not less than 300,000.

CAPSULES PENICILLIN IN OIL

Capsules penicillin in oil is a suspension of sodium penicillin or calcium penicillin in refined vegetable food oil. The potency of each capsule is not less than 20,000 units, and the number of capsules in each single package is such that the total number of units therein is not less than 300,000.

PENICILLIN WITH ALUMINUM HYDROXIDE GEL

Penicillin with aluminum hydroxide gel is a combination package of sodium penicillin or calcium penicillin and aluminum hydroxide gel. The quantity of aluminum hydroxide gel packaged with the penicillin shall be 30 cc. for each 100,000 units.

Indications and Dosage.—Oral penicillin preparations should be administered on a fasting stomach, not less than thirty minutes before or not less than one and one-half to two hours after eating.

Gonorrhea.—Combined Therapy: A single injection of 100,000 units followed not later than two or three hours by oral doses of 40,000 to 50,000 units each every two or three hours for six doses per day for one or two days.

Oral Therapy: Forty thousand to 50,000 units every two or three hours for six doses per day for one or two days.

In complications such as arthritis, endocarditis and epididymitis, administer penicillin parenterally. Concurrent infections of gonorrhea and syphilis should always be considered. Treatment of gonorrhea under the foregoing dosage schedule may prevent the appearance of the chancre and thus mask the first evidence of syphilis. The masking of the chancre should not be construed as a beneficial effect. Blood serologic tests should be made once a month for a minimum of three months.

Pneumococcic, Streptococcic and Staphylococcic Infections.—A minimum of 20,000 to 40,000 units of penicillin parenterally every three hours. After the acute phase and when the temperature has been reduced, treatment may be continued with oral administration. Treat with a dosage of 40,000 to 50,000 units each two or three hours (day and night) for at least forty-eight hours after the temperature has returned to normal. If the condition is not controlled by oral penicillin, return to parenteral administration.

Prophylaxis.—Against secondary infections after tonsillectomy or tooth extraction in cases with a history of rheumatic fever or rheumatic heart disease, congenital heart disease and other conditions in which secondary infections may occur (infected teeth or tonsils), administer 100,000 to 200,000 units daily in divided doses from one day before to three or four days after surgery.

Precautions.—In meningitis, endocarditis and peritonitis, administer penicillin *only* parenterally. In acute infection with bacteremia or septicemia, parenteral administration of penicillin should be continued until the blood cultures become negative and the acute condition is controlled. Do not use in those conditions listed in group III and IV under "Sodium Penicillin" and "Calcium Penicillin."

TOPICAL PRODUCTS

PENICILLIN OINTMENT; PENICILLIN OINTMENT OPHTHALMIC

Penicillin ointment is calcium penicillin in an ointment base composed of wool fat, petrolatum or white petrolatum, or any mixture of two or all of these with or without liquid petrolatum, white wax, yellow wax, cottonseed oil or peanut oil, or any mixture of two or all of these. Its potency is not less than 250 units per gram, and it contains not more than 50 viable micro-organisms per gram.

Penicillin ointment is packaged in collapsible tubes, not larger than 1 ounce size, except that ophthalmic ointments shall be in tubes not larger than the one-eighth ounce size.

PENICILLIN OINTMENT OPHTHALMIC

Indications and Dosage.—Superficial infections of the eye involving the cornea, conjunctiva, meibomian glands and lacrimal sac caused by organisms susceptible to penicillin. Apply one or more times a day as the condition indicates. Supplement local treatment of gonorrheal conjunctivitis with parenteral administration of penicillin.

Precaution.—If sensitization occurs, discontinue use.

PENICILLIN OINTMENT

Indications and Dosage.—Superficial infections of the skin caused by organisms susceptible to penicillin. Apply locally, with or without a bandage, one or more times a day as the condition indicates. If indicated, supplement local treatment with parenteral or oral administration of penicillin.

Precaution.—If sensitization occurs, discontinue use.

TOPICAL PENICILLIN

Topical penicillin is calcium penicillin which conforms to the standards prescribed therefor under "Calcium Penicillin" but is a fine powder. It may be packaged in vials or in foil enclosures containing not less than 10,000 units or not more than 50,000 units of penicillin.

Indications and Dosage.—For postoperative mastoid infections, inject through a small inlying catheter, directly into the cavity, 1 cc. of a sterile solution containing 50,000 units, once a day for a minimum of four days. In osteomyelitis, parenteral therapy may be supplemented by local instillation with 25,000 to 50,000 units in sterile solution two to three times a day. In empyema after aspiration, instil from 50,000 to 100,000 units into the cavity in a volume of solution less than the quantity of fluid aspirated. In superficial infections of the skin caused by organisms susceptible to penicillin, apply sterile dressings wet with a solution containing 1,000 units per cubic centimeter one or more times per day as the condition indicates. If indicated, supplement local therapy with systemic medication.

Precaution.—If sensitization occurs, discontinue use.

PENICILLIN TROCHES

Penicillin troches are composed of sodium penicillin or calcium penicillin and may contain masticatory substances. The potency of each troche is not less than 500 units. If the product contains masticatory substances, the word "chewing" or "masticatory" shall appear in juxtaposition with the name penicillin troches wherever such name appears on the label and labeling.

Indications and Dosage.—In Vincent's infection, allow one troche to dissolve in the mouth. Repeat two or three times a day between meals. Smears should be taken before and after therapy. If indicated, supplement local treatment with parenteral or oral administration of penicillin.

Precaution.—If sensitization occurs, discontinue use.

PENICILLIN TROCHES (MASTICATORY)

Indications and Dosage.—In Vincent's infection, chew two or three troches a day. When high continuous concentrations are desired, chew one troche each hour or two.

Precaution.—If sensitization occurs, discontinue use.

PENICILLIN DENTAL CONES

Penicillin dental cones are composed of calcium penicillin and may also contain sulfanilamide or sulfathiazole or both. The potency of each cone is not less than 500 units, and the content of viable micro-organisms is not more than 50 per gram. If a sulfonamide is used, its quantity is not less than 0.032 Gm. per cone.

Indications and Dosage.—Insert a cone after tooth extraction or as treatment for dry socket. Use in conjunction with parenteral therapy in operative procedures.

Precaution.—If sensitization occurs, discontinue use.

Awareness of Aging.—The subjective appraisal of failing physiologic and psychologic functions is largely an individual matter and is relative to cultural pressures and level of aspiration. Malamud points out that there is no one-to-one relationship between these different aspects of senile decline. Many of the psychologic traits of the aged are due to the cumulative effects of experience, to frustrations and the awareness of limitations, rather than to any primary or essential consequences of physiologic deficit.—Jones, Harold E., and Kaplan, Oscar J.: Psychologic Aspects of Mental Disorders in Later Life, from Mental Disorders in Later Life, edited by Oscar J. Kaplan, Stanford University Press, 1945.

Council on Physical Medicine

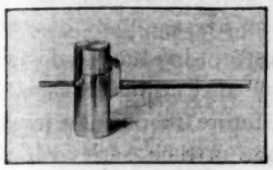
The Council on Physical Medicine has authorized publication of the following reports. HOWARD A. CARTER, *Secretary.*

TORPIN INSUFFLATOR ACCEPTABLE

Distributors: University of Georgia School of Medicine.

This device is designed to aid in the resuscitation of the cyanotic newborn. It is essentially a combination of a liquid trap and safety valve. The pressure of oxygen or air administered to the infant's lungs is controlled at all times by the weighted valve, which blows off at 20 cm. of water pressure. The trap acts as a reservoir for aspiration of mucus and other secretions from the trachea and also as a trap for the expiratory secretions of the operator. A reprint of an article entitled "Apnea Neonatorum" by Perry P. Volpitto and Richard Torpin, submitted as part of the evidence, describes the instrument and explains how it is used.

The device was investigated in a laboratory acceptable to the Council. It was reported as a metal trap designed to be inserted between the lips of the physician and a tube in the infant's trachea. If one sucks on the device, the trap serves to keep one from sucking material into one's mouth, and the heavy lid on the trap will be raised if one blows with too high a pressure. This will prevent blowing up the infant's lungs unduly. If the physician attaches the appliance directly to a tank of oxygen under high pressure instead of to his mouth, it will allow oxygen to escape rather than let it go into the trachea under high pressure. This is a desirable safeguard. The apparatus is harmless in its potentialities. The insufflator has been manufactured for the University of Georgia, which so far has aided in its distribution.



Torpin Insufflator.

The Council on Physical Medicine voted to accept this product for inclusion in its list of accepted devices.

KREISELMAN RESUSCITATORS, ADULT CART MODELS, ACCEPTABLE

Manufacturer: The Ohio Chemical & Manufacturing Company, 1177 Marquette Street, Cleveland.

Kreiselman resuscitators are designed for the administration of artificial respiration with oxygen to patients whose spontaneous respirations have not been resumed. These models are primarily for use in medical institutions. Essential parts of the apparatus are a two stage automatic reducing valve and an adjustable automat for regulating the amount of positive pressure exerted at the face piece, a flowmeter calibrated for oxygen, a flowmeter control valve, a resuscitation inhaler and tubing. These units are mounted on an upright stand equipped with three wheels. The shipping weight is approximately 175 pounds. Only positive pressure is provided by the apparatus. There is no negative pressure developed at the face piece. The units come equipped with tools and instructions.

Kreiselman Resuscitator, Model 61-A.

Model 61-A, which is essentially similar to the others, was furnished for investigation. The Council investigator reported that the pressure regulator is standard for the company and is reliable. The fitting of the oxygen cylinder is made for a "commercial" cylinder, and an adapter is furnished to fit "medical" cylinders. The apparatus provides a pressure at the face mask varying up to 25 mm. of mercury. The gas is delivered by pressing on a convenient lever with the thumb of the hand which holds the face mask. The mask can be removed and a fitting for an endotracheal tube substituted. When attached to either mask or tube, double valves permit normal inspiration and expiration to take place through it when the inflation lever is not pressed.

A second mask receives oxygen through another tube by way of a standard Heidbrink flowmeter graduated up to 14 liters of helium-oxygen mixture or 11 liters of pure oxygen. This second mask is open around the oxygen inlet so that free respiration of air can take place with the mask held in place in case the flow of oxygen is inadequate.

Both the inflator and the inhalator are commendably safe since, if no oxygen is available, the patient can continue to breathe normally.

A motor with the air pump is mounted on the cart which provides adequate negative pressure to suck mucus from the throat of a patient. This part of the apparatus seems safe. Doubtless the motor and the pump are the best available at present. This apparatus complete will, it is believed, serve the purpose for which it is intended both safely and efficiently.

Other Kreiselman resuscitators are acceptable since they are variations in assembly of otherwise accepted parts. The parts are in different combinations. They are Models Nos. 52, 52-A, 52-B, 61, 61-A, 61-B, 80, 80J, 81 and 81J.

The Council on Physical Medicine voted to adopt the Kreiselman resuscitators, models aforementioned, for inclusion in its list of accepted devices.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

ALUMINUM HYDROXIDE GEL (See New and Nonofficial Remedies, 1944, p. 382).

The following dosage forms have been accepted:

BARLOW-MANEY LABORATORIES, CEDAR RAPIDS, IOWA

Aluminum Hydroxide Gel: 480 cc. bottles. Contains the equivalent of 3.6 to 4.4 per cent of aluminum oxide (U. S. P. XII).

THE UPJOHN COMPANY, KALAMAZOO, MICH.

Aluminum Hydroxide Gel: 240 cc. and 3,840 cc. bottles. Contains the equivalent of 3.6 to 4.4 per cent of aluminum oxide (U. S. P. XII).

E. R. SQUIBB & SONS, NEW YORK

Aluminum Hydroxide Gel: 360 cc. and 3,840 cc. bottles. Contains the equivalent of 3.6 to 4.4 per cent of aluminum oxide (U. S. P. XII).

SYRINGE APPLICATORS FOR CONTRACEPTIVE JELLIES AND CREAMS (See New and Nonofficial Remedies, 1944, p. 341).

The following product has been accepted:

CONTRA CREME AND DIAPHRAGM CO., SEVERNA PARK, MD.

Contra Applicator: A transparent plastic syringe threaded at the blunt, intravaginal end, to screw onto the tubes of Contra Creme, to permit filling by compression of the tube. The full capacity is 5 cc., the recommended dose.

EPHEDRINE SULFATE (See New and Nonofficial Remedies, 1945, p. 270).

The following dosage form has been accepted:

THE WM. S. MERRELL CO., LOESER LABORATORY DIVISION, CINCINNATI

Solution Ephedrine Sulfate: 0.048 Gm. in 1 cc. ampuls.

DIETHYLSTILBESTROL (See New and Nonofficial Remedies, 1944, p. 417).

The following dosage form has been accepted:

WALLACE & TIERNAN PRODUCTS, INC., BELLEVILLE, N. J.

Tablets Diethylstilbestrol: 0.1 mg., 0.5 mg. and 1.0 mg.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, AUGUST 18, 1945

PENICILLIN IN SUBACUTE BACTERIAL ENDOCARDITIS

The therapy of subacute bacterial endocarditis, prior to the advent of the new chemotherapeutic agents, was all but futile. According to Libman, spontaneous recoveries probably occurred in from 3 to 5 per cent of the cases. Kelson and White [1] collected data on 66 cases treated intensively with sulfapyridine, and in 65 the course of the disease was not influenced by this therapy. Friedman, Hamburger and Katz [2] suggested that continued deposition of new fibrin and platelets on the vegetations created an impenetrable barrier to the action of otherwise effective agents; they proposed that a patient with bacterial endocarditis be first subjected to treatment with an anticoagulant such as heparin. Kelson and White [1] treated 7 patients with sulfapyridine and heparin. Only 3 patients were able to take heparin for more than a week, and in these there was a striking improvement. The first reports on the effect of penicillin in bacterial endocarditis were not encouraging. In the 17 cases reported by Keefer [3] there were four deaths during the course of treatment; in 3 cases temporary improvement was followed by a relapse in 2 soon after treatment was discontinued; no appreciable effect was noted in 10.

In contrast to these discouraging results, Loewe [4] reports a clinical cure in 75 per cent of a consecutive series of 54 unselected cases from a combined penicillin and heparin therapy. Loewe and his collaborators were able to limit the deposition of fibrin and platelets on the heart valves in animals with artificially induced bacterial endocarditis by administration of heparin. Friedman, McLean and others called attention to the difficulties and hazards of heparin therapy in man. Loewe and Rosenblatt [5] deposited the drug subcutaneously, utilizing the Pitkin menstruum, which is composed of gelatin, dextrose, glacial acetic acid and water in definite proportions. By this technic a slower and more equable absorption of heparin was accomplished. Loewe and his co-workers administered heparin and sulfonamide compounds combined to 17 patients with subacute bacterial endocarditis but could not determine an appreciable effect on the course of the disease in 15. Of the 54 patients treated with penicillin and heparin combined, 14 were failures and 40 appeared to be cured. In the latter group 37 are alive and many have resumed useful occupations; 3 have died of other causes. In the group of failures of treatment, thirteen deaths followed circulatory failure, coronary occlusion, embolization and pneumonia. These authors feel that a five week course of treatment with penicillin should be the standard minimum. Additional courses are well tolerated and are to be given when indicated. Based on penicillin sensitivity tests, an average daily dose of 200,000 Oxford units is suggested. Inadequate dosage invites failure, and the organisms may acquire resistance that is so high as to render future therapeutic levels unattainable. The total unitage in their series varied between the low 86,700 and a high of 48,930,000 Oxford units. To heparinize the blood effectually required subcutaneous deposition of 300 mg. of heparin every second or third day.

Dawson and Hunter [6] administered combined heparin-penicillin therapy to 16 patients with bacterial endocarditis. The infection of 11 patients has apparently been terminated. All 11 have remained bacteria free and in excellent health for three months or longer since treatment was discontinued. The infection of 2 patients was controlled but recurred when treatment was stopped. Two patients died as the result of a cerebral embolism. These authors feel that patients with subacute bacterial endocarditis should be treated with penicillin if the infecting organism is a streptococcus sensitive to the action of the drug. They were impressed with the advantages of administering penicillin by continuous intramuscular drip, as advocated by Harris.[7]

Bloomfield [8] and his associates obtained excellent results from intensive penicillin therapy alone carried on for six to eight weeks. All 11 patients were promptly made bacteria free except 1, who died early in the course of treatment. Eight were clinically cured of the infection after follow-up periods up to six months. One patient, apparently cured of the infection, died of cardiac failure. There were no clinical relapses or rein-

1. Kelson, S. R., and White, P. D.: New Method of Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **113:** 1700 (Nov. 4) 1939.
2. Friedman, Meyer; Hamburger, W. W., and Katz, L. N.: Use of Heparin in Subacute Bacterial Endocarditis, J. A. M. A. **113:** 1702 (Nov. 4) 1939.
3. Keefer, C. S.; Blake, F. G.; Marshall, E. K., Jr.; Lockwood, J. S., and Wood, W. Barry, Jr.: Penicillin in the Treatment of Infections, J. A. M. A. **122:** 1217 (Aug. 28) 1943.
4. Loewe, Leo: Combined Use of Anti-Infectives and Anticoagulants in Treatment of Subacute Bacterial Endocarditis, Bull. New York Acad. Med. **21:** 59 (Feb.) 1945.
5. Loewe, Leo, and Rosenblatt, Philip: A New Practical Method of Subcutaneous Administration of Heparin, Am. J. M. Sc. **208:** 54 (July) 1944.
6. Dawson, M. H., and Hunter, T. H.: Treatment of Subacute Bacterial Endocarditis with Penicillin, J. A. M. A. **127:** 129 (Jan. 20) 1945.
7. Harris, F. I.: Continuous Intramuscular Infusion of Penicillin, J. A. M. A. **126:** 232 (Sept. 23) 1944.
8. Bloomfield, A. L.: Treatment of Subacute Bacterial Endocarditis with Penicillin, J. Clin. Investigation **24:** 251 (May) 1945.

fections. These authors believe that the time factor is even more important than the daily dose. The failures of the early attempts were due to short periods of treatment. Continuous treatment over long periods is more likely to eradicate the infection than brief courses of penicillin.

CULTIVATION OF MALARIAL PARASITES

In 1912 Bass and Johns [1] reported a method for the cultivation of two species of malarial parasites of man. Blood drawn from a malarial patient was expelled directly into a defibrinating tube containing 0.1 cc. of a 50 per cent dextrose solution for each 10 cc. of blood taken. Defibrination was effected by gentle stirring with a glass rod. The defibrinated blood was allowed to sediment at incubator temperature (40 C.) until a column of serum ½ to 1 inch deep was above the sedimented cells. The parasites live and develop in the half millimeter top layer of the sedimented cells. All parasites beneath this top layer die and disintegrate. In such a culture the young parasites increase in size during the first twenty-four hours. Segmentation begins in about thirty-six hours. Extracellular parasites are rapidly ingested and destroyed by leukocytes. A free asexual malarial parasite cannot live longer than a few minutes in normal human serum. Probably, therefore, malarial plasmodia can pass from cell to cell only when the cells are in direct contact.

Most of the earlier investigators [2] who attempted to confirm this work reported that development of human malaria parasites in the so-called culture is at best only minimal. Counts show that increases do not occur in the number of parasites. Other investigators afterward applied a modification of this technic to the attempted cultivation of malaria parasites from canaries, domestic fowls and monkeys. Among the most favorable results were those reported by Gavrilov,[3] who showed that tissue cultures from the bone marrow of chickens infected with Plasmodium gallinacium remained infective for ten days. Trager [4] of the Rockefeller Institute effected in vitro survival of the bird malarial parasite (Plasmodium lophurae) up to sixteen days. The parasite population in his "cultures" usually remained constant for the first few days and then declined. He concluded that the death rate, particularly after the first few days, far exceeded the birth rate, though development must have been continuing in his preparations.

A much more successful in vitro cultivation of malarial parasites is now reported by Ball and his co-workers [5] of Harvard Medical School. They selected the erythrocytic form of Plasmodium knowlesi, a malaria parasite of monkeys (Macaca mulatta), which also produces infection in man. This parasite has a twenty-four hour asexual life cycle. They first developed a buffered nutrient fluid consisting of glucose (2.5 Gm. per liter), proteose peptone (1.5 Gm.), a purified mixture of amino acids (0.5 Gm.) and the usual salts necessary for tissue cultures, supplemented by presumably optimal amounts of all known essential vitamins.

Two culture technics were developed. By the first, or "rocker dilution," technic 1 part of whole malarial blood was added to 3 parts of nutrient fluid, and the mixture was placed in a flask equipped with a gas inlet and outlet. The container was placed in a rocker machine, which just kept the red cells in suspension. A slow flow of 5 per cent carbon dioxide in 95 per cent air was passed through the container. The whole procedure was carried out with aseptic precautions at a temperature of 38.5 C. The best results were obtained when the number of parasitized cells in the mixture was not more than 25,000 per cubic millimeter. More highly parasitized blood was diluted with several times its volume of normal monkey blood.

The second, or "rocker perfusion," technic employed a cellophane membrane to separate the infected blood from the nutrient medium. Several types of apparatus were developed. For small volumes of blood the cellophane membrane was stretched over one end of a glass tube about 1 inch in diameter. The blood was placed within the tube directly on the membrane. The tube was mounted in a vessel containing the nutrient fluid so that the membrane was just wet by the fluid. For larger cultures a coil of cellophane tubing was used. This was supported by a glass form and immersed in the blood. Nutrient fluid was allowed to flow through the tubing at a rate of approximately 1 cc. per minute. In both types of cultivation a slow stream of 5 per cent carbon dioxide in 95 per cent air was passed through the container, which was gently rocked to keep the corpuscles in suspension. All operations were performed at 38.5 C.

Cultivation was usually carried on for twenty-four hours. If subcultures were desired, a fresh setup was made at the end of each twenty-four hours, the parasitized blood being diluted with normal blood and the nutrient fluid replaced. The addition of one fourth volume of normal blood serum to the nutrient fluid was an advantage. In eighty-nine experiments the average increase in parasite count within twenty-four hours was approximately fourfold. In 60 monkeys the average in vivo increase in parasite count for the same period was also fourfold. Differential counts during the twenty-four hour period showed that segmentation usually takes place between the fifth and the tenth hour.

Under the rocker perfusion technic six successive generations have thus far been cultivated by the Harvard pathologists. The infectivity of the sixth genera-

1. Bass, C. C., and Johns, F. M.: J. Exper. Med. **16**: 567, 1912.
2. Horovitz, A., and Sautet, J.: Ann. Parasitol. **7**: 151, 1929.
3. Gavrilov, W.; Bobkoff, G., and Laurencin, S.: Ann. Soc. belge méd. trop. **18**: 429, 1938.
4. Trager, William: J. Exper. Med. **74**: 441, 1941; **77**: 411, 1943.
5. Ball, E. G.; Anfinsen, C. B.; Geiman, Q. M.; McKee, R. W., and Ormsbee, R. A.: Science **101**: 542 (May 25) 1945.

tion was demonstrated by inoculation into a monkey. The technic is now being applied with encouraging results to the in vitro cultivation of human malaria parasites. Typical of results thus far obtained is their finding that para-aminobenzoic acid is probably the chief essential growth component furnished by the nutrient fluid. This in their opinion may help to explain the observation of Coggeshall [6] that sulfanilamide will eradicate P. knowlesi infections in monkeys.

UNAVAILABLE NUTRIENTS

After the discovery of the vitamins it became obvious that a conventional chemical analysis of a food might give little indication of its real nutritive value, as the relative quantities of these accessory food factors usually are too small to be thus measured. As time passed it became increasingly plain that a similar philosophy applies to dietary constituents which can be measured; in addition to a chemical analysis, the utilization of these constituents can be examined by the methods of biologic assay. Through this device it has been shown that a wide variation exists in the availability to the organism of dietary essentials in various forms in our foods. A relatively simple method of determining the availability of iron, for instance, is to measure hemoglobin regeneration in an animal on an iron free diet to which the source of iron to be tested is added. Sherman, Elvehjem and Hart [1] found that about 70 per cent of the iron of liver is available for hemoglobin formation but only 50 per cent of that in wheat can be used and only 20 per cent of the total iron of spinach is utilized. Nakamura and Mitchell [2] examined some pure iron compounds and found that the iron of ferric phytate was only about one half as available to the rat as ferric chloride. The presence of phytate is believed to explain the low utilization of the iron of whole wheat.

In studying the calcium utilization of high extraction flour, that is, the dark flour which contains most of the wheat kernel, McCance and Widdowson [3] observed that the calcium of 92 per cent extraction flour was less completely used by human subjects than was the calcium in 69 per cent extraction flour (white flour). Addition of sodium phytate to the white flour depressed the availability of calcium in the product. In a white flour to which dephytinized bran was added to simulate a synthetic high extraction flour, the calcium was as available as in the original white flour. Hence the factor in whole wheat which renders its calcium unavailable is believed to be phytic acid.

Earlier investigations have shown that both human beings and experimental animals are unable to utilize the thiamine from fresh yeast as completely as that present in dried or dead yeast samples. Recently Parsons, Williamson and Johnson [4] have presented data on human subjects which show that the thiamine present in two types of commercial bakers' yeast was not utilized when the yeast was fed in the fresh state. This was indicated by a high fecal and low urinary excretion of thiamine. In addition, ingestion of these yeasts reduced the availability of thiamine which was supplied by the basal diet. By boiling the yeast for a short time before ingestion, the availability of the thiamine present in the yeast cells was strikingly increased. Although a different species of yeast with a higher thiamine content did not show the inhibition of utilization of dietary thiamine, boiling this yeast also made its thiamine more available. Thus it appears that fresh yeast is not as reliable a source of thiamine as is heat-treated yeast.

Evidently the total content of a nutrient in a food is not the only index to its nutritional value; of equal or more importance is the ability of the animal to utilize the nutrient. Tables of nutritive factors in foods will no doubt soon give the available or utilizable nutrients rather than the total nutrients as shown by chemical analysis. Such tables would be especially valuable to the physician who is planning adequate therapeutic diets.

Current Comment

DIAGNOSIS OF PULMONARY TUBERCULOSIS IN THE ADULT

In a recent essay on primary principles for guidance in the diagnosis of tuberculosis of the lungs Pinner [1] emphasizes the need of a better understanding by the public of the possible significance of minimal symptoms and the importance of proper examination of the patient. In pulmonary tuberculosis, as also in cancer, the advanced stage of the disease when the patient comes under treatment is the greatest hindrance to its success. In both instances the fault may lie with the patient who fails to seek treatment early or with the physician who fails in his diagnosis. Pinner points out that periodic x-ray examination, which is the only means of discovering pulmonary tuberculosis in a prognostically hopeful stage, is not yet practiced as promptly and widely as its value demands. He urges more and wider x-ray surveys, especially in groups in which tuberculosis is prevalent. The preemployment examinations, including x-ray films, which have proved of great value in defense industries should be continued and followed by earnest efforts at physical and economic rehabilitation. The lack of such efforts is "probably the weakest link

6. Coggeshall, L. T.: J. Exper. Med. **71**: 13, 1940.

1. Sherman, W. C.; Elvehjem, C. A., and Hart, E. B.: J. Biol. Chem. **107**: 383 (Nov.) 1934.

2. Nakamura, F. I., and Mitchell, H. H.: J. Nutrition **25**: 39 (Jan.) 1943.

3. McCance, R. A., and Widdowson, E. M.: J. Physiol. **101**: 44 (June 2); 304 (Nov. 30) 1942.

4. Parsons, H. T.; Williamson, A., and Johnson, M.: J. Nutrition **29**: 373 (June) 1945.

1. Pinner, Max: Pulmonary Tuberculosis in the Adult, Springfield, Ill., Charles C Thomas, 1945, p. 347.

in our present antituberculosis work." In his discussion of the actual diagnosis of pulmonary tuberculosis in a case Pinner makes it clear that the question is to determine whether or not an active tuberculous focus is present in the lungs. Here the value of the tuberculin test will depend on the reactor rate of the group to which the patient belongs. The test would hardly be worth while in cities where that rate is close to 100 per cent in adults. While the presence of a focus of disease in the lungs may be demonstrable by physical examination, physicians should remember that absence of a focus cannot be determined without proper x-ray examination. The patient cannot be assured that he does not have pulmonary tuberculosis except on the basis of such examination. Establishment that a focus in the lungs is actively tuberculous requires the demonstration of tubercle bacilli in the sputum or in the gastric contents. If bacilli cannot be found in the presence of a suspected focus, all the differential diagnostic possibilities must be considered. The demonstration of tubercle bacilli, changes on serial roentgenograms and pulmonary symptoms establish active tuberculosis, but the absence of any one of these criteria does not exclude activity. The decision may require prolonged observation. In recent years the examinations on military induction, before employment and in diagnostic surveys are bringing to light so-called asymptomatic patients in whom pulmonary lesions are discovered accidentally. Here the problem of differential diagnosis and tuberculous activity requires special study. In Pinner's hands serial roentgenograms, bacterial tests and close study of symptoms have given good results, while hematologic data have been of relatively low value. In view of the fundamental importance of the x-ray examination in the recognition of pulmonary tuberculosis, provision should be made everywhere for competent free examination of patients who are unable to pay. Fortunately this is now done in many cities. The importance of early correct diagnosis cannot be overstated, because "symptomatic treatment without adequate diagnosis is a prominent cause of far advanced tuberculosis."

STAIRWAYS AND THE PHYSICALLY HANDICAPPED

The National Society for Crippled Children and Adults has recently inaugurated a campaign to construct new public buildings with ground level entries, elevators between floors and the elimination of all unnecessary steps. This society also urges the remodeling of existing buildings with long flights of stairs, to provide ground level entries, elevators, ramps and other practicable measures aimed at the elimination or amelioration of impediments to ready access. Patients with heart disease, crippling illnesses, missing limbs or other disorders of locomotion form an increasing proportion of the population, both because of the war and because of the lengthened average age. Progress along the lines suggested should decrease the number of accidents among the handicapped as well as greatly increase their ability to perform business activities and seek pleasure with greater frequency and ease.

THE SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH

In connection with the expansion of the Memorial Hospital in New York City the Alfred P. Sloan Foundation has announced the appropriation of $4,000,000 for the erection and initial maintenance of the Sloan-Kettering Institute for Cancer Research. The building will stand in the middle of the "Memorial Cancer Center." The cost of construction is estimated at $2,000,000, and $200,000 a year will be provided for running expenses for ten years. The clinical facilities and materials of the center will be available to the institute, which will have its own board of trustees and be "self contained in all its various research functions." The present research organization of the hospital will become part of the institute. To complete the plans for the expansion of the Memorial Hospital an additional $3,000,000 to $4,000,000 will be needed for increase of its bed capacity, for training fellowships and for the equipment of the James Ewing Hospital of 300 beds to be built by the city of New York on the same grounds. The completion of this program will result in the creation of a great center for cancer service and cancer research, a model for the establishment of similar centers in other cities. Commenting on the projected institute Mr. Alfred P. Sloan Jr., the sponsor of the foundation, said that his industrial experience has led him to appreciate the amazing possibilities of research when organized on a broad and comprehensive scale and that he and his associate, Dr. Charles F. Kettering, are convinced of the applicability of the broad principles of organized industrial research to the problems of cancer. "The current acceleration of scientific knowledge provides an unusual opportunity for a determined all-out effort." Mr. Sloan also said "In addition to this specific project we hope it may be possible to organize on a high scientific level the more complete coordination of other worthy efforts now being directed to the same end objective. It is of great importance that this be done. It should result in a more effective use of aggregate resources now available for the purpose." This is indeed tidings of momentous significance. Solution of the problems of cancer can be attained only by research. The new institute will carry on its work in the spirit and the conviction that long-range programs of research with adequate support and direction can solve such problems. At the same time the control of cancer by the means at hand will be steadily promoted by improving and enlarging the facilities for skilled clinical service coupled with continuous education of the public in the vital importance of early and effective treatment.

MEDICINE AND THE WAR

TRANSPORTABLE SICK AND WOUNDED SOLDIERS HOME FROM EUROPE

The War Department recently announced that the Army's plan for bringing all transportable sick and wounded soldiers home from Europe within ninety days after V-E day will be completed according to schedule. To achieve this ninety-day goal army authorities put on such pressure, beginning with V-E day, that the major portion of the task was done within sixty days. This is in sharp contrast to the procedure in the first world war, when American sick and wounded soldiers remained overseas about a year.

In May there were more than 43,000 soldiers brought home from the European theaters, practically all after May 8, or V-E day. With approximately 14,000 who came into West Coast hospitals, this brought the May total to an all time high of approximately 57,000 who were evacuated. The figure for evacuees from Europe dropped the next month to slightly less than 32,000, which, with the Pacific casualties, made the evacuation total over 42,000 for June. In July approximately 27,000 arrived at East Coast ports, which included practically all of those who were wounded prior to V-E day. The number of nontransportable cases is comparatively small, Brig. Gen. Raymond W. Bliss, assistant Surgeon General of the Army, said.

The nation's wounded and sick servicemen arrive under the care of army doctors, nurses and Medical Department personnel at New York, Charleston, S. C., Boston and Hampton Roads, Va. The majority are disembarked at the first two ports. It is only a matter of hours from the time these soldiers reach port until they are assigned a bed at a nearby hospital, such as Halloran General at New York or Stark General at Charleston.

At the time of Pearl Harbor there were approximately 15,000 beds in all army general hospitals in this country. The army general and convalescent bed capacity is now 215,000. This does not include the vast network of army station and regional hospitals which care for the routine needs of sick and wounded soldiers who have been incapacitated in this country.

CIVILIAN PSYCHIATRISTS COMPLETE ETO SURVEY

At the request of the Surgeon General, the Office of Scientific Research and Development appointed a group of noted civilian psychiatrists to undertake a study of combat exhaustion problems in the European Theater of Operations. These psychiatrists have now returned with a report of their findings. Included in the group which made the survey with the cooperation of the Army Medical Department are Dr. Leo H. Bartemeier, professor of psychiatry, Wayne University, Detroit; Dr. Lawrence S. Kubie, associate in neurology, Columbia University College of Physicians and Surgeons, New York; Dr. Karl Menninger, director of the Menninger Clinic, Topeka, Kan.; Dr. John Romano, professor of psychiatry, Cincinnati General Hospital, Cincinnati, and Dr. John C. Whitehorn, chief psychiatrist of Johns Hopkins Hospital and professor of psychiatry, Johns Hopkins University School of Medicine, Baltimore.

AWARDS MADE FOR YUGOSLAV TYPHUS WORK

Brig. Gen. Leon Fox, Birmingham, Ala., chief of the United States Typhus Commission, and three members of his staff were recently awarded the Yugoslav medal for services to the people of Yugoslavia. Two of the awards were given to Lieut. Col. Edward Murray, Cedar Rapids, Iowa, and Lieut. Col. Charles Wheeler, Doon, Iowa.

95TH STATION HOSPITAL AWARDED PLAQUE

The Meritorious Service Unit Plaque was recently awarded to the 95th Station Hospital "for superior performance of duty in the completion of exceptionally difficult tasks under adverse conditions and the maintenance of a high standard of military discipline and efficiency during the period Oct. 15, 1944 to Feb. 15, 1945." Col. A. A. Leonidoff is commanding officer of the hospital, and Major James W. Tobin and Lieut. Col. Charles D. Driscoll are chief of surgical service and chief of medical service, respectively.

DR. A. L. BENISON REPORTED MISSING

Dr. A. L. Benison, formerly of Edmore, Mich., serving in the U. S. Army and captured by the Japanese at Pearl Harbor, is reported lost on a Japanese prison ship 200 miles off the coast of China. The ship was reported to have been torpedoed by submarines as it was taking American war prisoners to Japan last October 24. Dr. Benison graduated from the University of Michigan Medical School, Ann Arbor, in 1937 and entered the service May 15, 1941.

ARMY AWARDS AND COMMENDATIONS

Colonel Clifford V. Morgan

A Bronze Oak Leaf Cluster to the Legion of Merit was recently awarded to Col. Clifford V. Morgan, formerly of Washington, D. C. The citation accompanying the award read "for exceptionally meritorious conduct in the performance of outstanding services, as deputy general purchasing agent, Forward Echelon, Headquarters Communications Zone, European Theater of Operations, from Feb. 25, 1944 to Aug. 7, 1944. Colonel Morgan supervised and coordinated general purchasing planning as far as coordination was necessary with 21st Army Group (British), First United States Army Group, First United States Army, Third United States Army, Western Task Force, 9th Air Force, and agencies of Communications Zone staff. He ably guided and facilitated purchasing planning for overseas operations and formulated a clear and concise general purchasing agent plan consistent with directives of higher authority. Colonel Morgan rendered outstanding services on the continent not only by advising and personally assisting the advance section, but also by attaching key personnel to that section for training purposes." Dr. Morgan graduated from the University of Nebraska College of Medicine, Omaha, in 1927 and has been in the service since August 1928.

Colonel Edward D. Churchill

The Legion of Merit was recently awarded to Col. Edward D. Churchill, formerly of Boston, "for exceptionally meritorious conduct in the performance of outstanding services. By instituting advanced principles of war surgery throughout American hospitals in the theater during the Tunisian campaign, and by initiating a standardized surgical technic, he was responsible to a considerable extent for the extremely low mortality rate among wounded soldiers. By his keen foresight, his efficient planning and careful supervision of surgical procedures, much suffering was alleviated and many lives were saved." Dr. Churchill graduated from Harvard Medical School, Boston, in 1920 and entered the service Jan. 10, 1943.

Major Donald Grillo

For his work in the activation and evacuation of his station hospital at Kweilin, China, Major Donald Grillo, formerly of Gary, Ind., was recently awarded the Bronze Star. Dr. Grillo graduated from Indiana University School of Medicine, Indianapolis, in 1929 and entered the service in July 1942.

Major Edward C. Dyer

The Bronze Star was recently presented to Major Edward C. Dyer, formerly of Boston, "for meritorious achievement in action during the period Feb. 19, 1945 to Feb. 25, 1945, near Monte Belvedere, Italy." Dr. Dyer graduated from Harvard Medical School, Boston, in 1939 and entered the service Feb. 17, 1942.

Major Harry DeWitt Nesmith

Major Harry DeWitt Nesmith, formerly of Salem, Ill., was recently awarded the Bronze Star for meritorious achievement in connection with military operations against the enemy from June 1, 1944 to March 31, 1945. At the present time he is stationed in Germany. Dr. Nesmith graduated from the University of Illinois College of Medicine, Chicago, in 1939 and entered the service in March 1941.

Major Hugh M. Crumay

The Air Medal was recently awarded to Major Hugh M. Crumay, formerly of Mercer, Pa. The citation accompanying the award read "For meritorious achievement while participating in the Southwest Pacific Area, during which hostile contact was probable and expected. The courage and devotion to duty shown during these fights are worthy of commendation." Dr. Crumay graduated from Harvard Medical School, Boston, in 1933 and entered the service July 17, 1942.

Captain David Paris

The Bronze Star was recently awarded to Capt. David Paris, formerly of Cushing, Okla., "for meritorious achievement in connection with military operations against the enemy at Aitape, British New Guinea, from July 1, 1944 to Sept. 9, 1944; at Morotai, Netherlands East Indies, from Sept. 15, 1944 to Nov. 9, 1944; at Leyte, Philippine Islands, from Nov. 14, 1944 to Jan. 22, 1945, and at Luzon, Philippine Islands, from Jan. 29, 1945 to June 1, 1945." Dr. Paris graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1941 and entered the service July 1, 1942.

Captain Robert L. Kendall

Capt. Robert L. Kendall, formerly of Ardmore, Okla., was recently awarded the Bronze Star "for meritorious service in direct support of combat operations from Aug. 15, 1944 to Jan. 15, 1945 in France. During this period Captain Kendall's station has operated under a variety of conditions ranging from rapid advances requiring a high degree of mobility to static conditions with a large number of casualties. Despite adverse circumstances, Captain Kendall obtained a high state of efficiency and standard of medical care. The problem of serving two additional regiments was handled promptly and efficiently under his direction." Dr. Kendall graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1940 and entered the service Jan. 6, 1942.

NAVY

THE NAVY MEDICAL OFFICERS INQUIRE ABOUT DISCHARGE

[NOTE.—*Recently a letter from five Army medical officers was published. Here follows a similar communication from five Navy medical officers.*—ED.]

To the Editor:—We are Navy medical officers on active duty for varying lengths of time ranging from forty-two to thirty months. Most of us have seen duty throughout the mid and southwest Pacific. Like our Army colleagues, we have given much thought to the problems of rotation and the staffing of veterans' hospitals after the war. We have two suggestions to make which we sincerely believe are practical and meritorious. Like our colleagues, we hope to be heard and we trust that you will publish this letter under conditions similar to those pertaining to the Army one.

There are hundreds of Navy reserve medical officers on active duty who are over 40 years of age and have served for over three years. Many of these are married and have families. Like firemen, they have been standing by their posts, often inactive for long periods of time. They are anxious to work and to use their medical skill where it is most needed.

There are hundreds of civilian physicians who are overworked, some of them for as much as fourteen hours a day, and have been overworked for several years. Without waiting for the cessation of hostilities, would it not be possible to have the Procurement and Assignment representative in each state relieve some of these overworked civilian physicians with relatively idle Navy medical officers? To effect the transfer in as close a location as was proper, Navy headquarters in each district could submit to P. & A. headquarters the names of reserve physicians over 40 years of age or who have had over three years' active service and who express a desire to be relieved. The civilian physician could be shown the ropes by one of the other Navy medical officers and, like many other civilian employees of the Navy, would not have to wear a uniform.

The staffing of larger temporary Naval hospitals and of veterans' hospitals after the war deserves grave consideration. A system similar to the foregoing could be adopted for a period of thirty-six months following the end of hostilities. Overworked civilian physicians could be assigned to such hospitals under a special classification by the state P. & A. director. (If civilians are strong enough to work extremely hard for twelve hours a day in private practice they will certainly be able to stand the less arduous duties of an eight hour day in a Naval or veterans' hospital; indeed, the change will benefit them.) It will be noted that this suggestion in no way interferes with the training of medical students, since it is not proposed that men essential for full time teaching be displaced. The basic proposal is for a fair rotation of civilian and military doctors for a three year period following the termination of hostilities; at the end of that time the matter can be reviewed and further equitable adjustments made.

MARINE CORPS' AMPHTRACKS EQUIPPED AS FIELD HOSPITAL

The Marine Corps' amphtracks are now fitted with the equipment of a field hospital and are serving as front line mobile operating rooms. Utilization of the hitherto strictly combat vehicle in its new role is the idea of Navy Capt. Joseph W. Kimbrough, formerly of San Francisco and now chief surgeon of the First Marine Division, who started work on the idea months before the invasion of Okinawa. Once the amphtrack moves into the desired site, the hospital gear is unpacked and set quickly into position. The metal interior is covered with white fabric, trays of surgical instruments are placed in a sterilizer and the portable operating table and lamp are set up. Then by means of the canvas covers carried as part of the regular equipment of the vehicle, blackout curtains are rigged so that the doctors can work throughout the night without fear of drawing enemy rifle or artillery fire.

HEAD OF POSTWAR PLANNING BOARD

Capt. William E. Eaton (MC), U.S.N. (Ret.), was recently relieved as head of the Washington Office, Materiel Division, Bureau of Medicine and Surgery, to devote full time to his duties as head of the Postwar Planning Board. Succeeding him in the materiel post is Lieut. Comdr. Paul T. Rees (HC), U.S.N., whom the Surgeon General also has nominated as representative of the Bureau of Medicine and Surgery to work with the logistics organization planning unit on the call of its senior member in the development of a Navy supply program.

COMMANDER EUGENE PERRY HARRIS

The Croix de Guerre with red star was recently awarded to Comdr. Eugene Perry Harris, formerly of Washington, D. C., by the government of France for exceptional war service rendered in the course of operations in the liberation of France for the period June to December 1944. Dr. Harris was previ-

ously awarded the Legion of Merit by our own government for his work during the same time interval. He is at present assigned to the U. S. Naval Hospital, Corvallis, Ore., as chief of the eye, ear, nose and throat service. Dr. Harris graduated from the University of Texas Medical Branch, Galveston, in 1930 and was commissioned in the Navy in January 1937.

NAVY AWARDS AND COMMENDATIONS

Lieutenant (jg) Leonard Hunter Roach

The Bronze Star was recently awarded to Lieut. (jg) Leonard Hunter Roach, formerly of St. Louis. The citation accompanying the award read "for heroic achievement as assistant battalion surgeon during action against enemy Japanese forces in the Marianas Islands, on Saipan from June 15 to July 10, 1944 and on Tinian from July 24 to Aug. 1, 1944. Courageous in the face of a heavy artillery and mortar barrage, Lieutenant, Junior Grade, Roach displayed outstanding professional skill and executive ability in evacuating casualties on the beach during initial landings on Saipan and, by his valiant devotion to duty during the invasion and occupation of these islands, continued to administer medical aid to wounded men, thereby materially reducing casualties under the extremely difficult combat conditions. His self-sacrificing spirit and gallant conduct were in keeping with the highest traditions of the United States Naval Service." Dr. Roach graduated from the University of Cincinnati College of Medicine in 1942 and entered the service May 3, 1943.

Lieutenant Frank Ashbrook Stewart

The Silver Star was recently awarded to Lieut. Frank Ashbrook Stewart, formerly of Stamford, Conn. The citation read "for conspicuous gallantry and intrepidity while serving with the 3d Battalion, 1st Marine Division during action against enemy Japanese forces at Cape Gloucester, New Britain, on Jan. 14, 1944. With his battalion engaged in routing a fanatic, deeply entrenched enemy from heavily fortified Hill 660, Lieutenant Stewart fearlessly risked his life in a valiant effort to aid marines who had fallen under the fierce opposition. Gallantly proceeding up the steep incline through enemy infested, unfamiliar jungle terrain, he skilfully and calmly cared for the wounded despite the enemy's shattering machine gun and rifle fire, carrying out his perilous task with undaunted initiative until evacuation could be effected. By his outstanding professional ability, determined perseverance and grave concern for the safety of others at great personal risk, Lieutenant Stewart contributed to the saving of many lives and upheld the highest traditions of the United States Naval Service." Dr. Stewart graduated from the University of Nebraska College of Medicine, Omaha, in 1940 and entered the service Feb. 8, 1943.

Lieutenant Commander Francis A. Agrest

Lieut. Comdr. Francis A. Agrest, formerly of Brooklyn, was recently awarded the Presidential Unit citation. Commander Agrest took part in three campaigns with the First Marine Division in the Southwest Pacific. He graduated from the Long Island College of Medicine, Brooklyn, in 1934 and entered the service March 29, 1941.

MISCELLANEOUS

EPIDEMICS OF RELAPSING FEVER

The extensive epidemics of typhus which swept North Africa during the war have been followed by an epidemic of louse borne relapsing fever. Dr. G. Stuart, chief of the Epidemic Control Section of the UNRRA European Regional Office, stated that more than 40,000 cases were reported up to March 1945, mainly in Tunisia, but in recent months the outbreak has spread also to Algeria and Morocco. After the first world war eastern Europe suffered from extensive epidemics of relapsing fever, and some twenty years ago this disease decimated the population of the semiarid country south of the North African desert belt. Lately there have been small outbreaks in southern France and in Rumania, but so far there has been no major epidemic in Europe.

UNRRA CONTRIBUTES FULLY EQUIPPED AMBULANCE

A fully equipped ambulance was recently turned over to the republic of San Marino by Lieut. Col. Vincent B. Lamoreux of the UNRRA Italian Mission Medical Division. This is the first contribution under the agreement signed recently with UNRRA whereby the small republic is to receive assistance up to $30,000. Medical supplies transported in the ambulance included penicillin, insulin, DDT insecticide powder, vitamin C tablets, ether, calcium gluconate ampules, phenobarbital tablets, sulfadiazine ointment, bandages, cotton gauze, suture catgut, syringes, thermometers, forceps, blankets, sheets, powdered and condensed milk, and sugar.

DDT ADDED TO INSECTICIDE MIXTURE

Addition of DDT to the Army's insecticide dispenser, known among troops in the Pacific as the aerosol bomb, has greatly increased the effectiveness of the insecticide mixture in that now it kills not only mosquitoes but also disease-bearing flies. The new mixture is composed of 85 per cent freon, 2 per cent of a 20 per cent pyrethrum solution, 5 per cent cyclehexanone, 5 per cent lubricating (hydrocarbon) oil and 3 per cent DDT. With DDT added, the aerosol bomb becomes an excellent weapon in the fight against malaria and fly-borne diseases.

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

California

Birmingham General Hospital, Van Nuys: Effects of High Altitude and Gravity, Prof. D. R. Drury, September 12; Cardiovascular Problems, Dr. W. Gordon Garnett, September 26.

Camp Cooke Station Hospital, Lompoc: Respiratory Disease Problems, Major F. E. Willett, September 5; War Wounds of the Chest, Lieut. Comdr. J. P. O'Connor and Lieut. Henry Jaffee, September 19.

A. S. F. Regional Hospital, Camp Haan: The Pneumonias, Dr. W. E. MacPherson, September 4.

Hoff General Hospital, Santa Barbara: Respiratory Disease Problems, Major F. E. Willett, September 5; War Wounds of the Chest, Lieut. Comdr. J. O. O'Connor and Lieut. Henry Jaffee, September 19.

A. A. F. Regional Station Hospital, March Field, Riverside: The Use of Fibrin and Fibrolysin in Wound Healing, Capt. Harry P. Schenck, September 18.

Santa Ana Army Air Base Regional and Convalescent Hospital, Santa Ana: Acoustic Trauma, Comdr. D. G. Mitchell, September 4; Rheumatic Heart Disease, Dr. Louis E. Martin, September 18.

Torney General Hospital, Palm Springs: Surgery of the Biliary Tract, Capt. Howard K. Gray, September 4; The Management of the Simple Skin Diseases, Lieut. Col. Everett R. Seale, September 18.

U. S. Naval Hospital, Santa Margarita Ranch, Oceanside: Cardiac Pain, Lieut. Comdr. Robert L. Langley, September 13; Differentiation Between the Protozoal and the Bacillary Dysenteries, Dr. John F. Kessel, September 27.

U. S. Naval Air Training Station, San Diego: Clinical Aspects of Rheumatic Fever, Lieut. Comdr. George C. Griffith, September 6; Problems in Tuberculosis, Comdr. W. L. Rogers, September 7; The Malingering Tests, Dr. John Mackenzie Brown and Mr. Raymond Brown, September 21.

U. S. Naval Hospital, Long Beach: Problems in Tuberculosis, Comdr. W. L. Rogers, September 19.

U. S. Naval Hospital, Corona: Allergy, Dr. John Lamson, September 13; The Rh Factor, Capt. George Macer, September 27.

ORGANIZATION SECTION

Bureau of Information

SUMMARY SHEETS FROM MONTANA AND NEBRASKA

Completed county summary sheets have been received from most of the counties in Montana and Nebraska through Dr. R. F. Peterson, secretary, Medical Association of Montana, and Dr. R. B. Adams, secretary, Nebraska State Medical Association.

The accompanying table gives data from selected counties in each of these states. The column giving the number of persons per telephone is used as one index of the economic status of the area. Many physicians over 65 years of age are carrying on large practices and are doing much to maintain the health of communities. They are not included in computing physician population ratio, however, as the future needs of the communities will be largely dependent on younger physicians.

Montana

County [1]	Principal Cities [2]	Population	Physicians Under 65	Persons per Physician	Persons per Telephone [3]
Big Horn		8,494	2	4,247	42
Blaine		7,739	4	1,935	33
Cascade		42,016	31	1,355	8
	Great Falls	29,928			
Deer Lodge		14,061	6	2,344	13
	Anaconda	11,004			
Garfield		1,999	1	1,999	0
Jefferson		3,444	1	3,444	19
Richland		8,737	3	2,912	18
	Sidney	2,978			
Rosebud		5,644	3	1,881	21
Stillwater		5,158	1	5,158	18
Yellowstone		37,907	26	1,458	8
	Billings	23,261			
	Laurels	2,754			

Nebraska

County [1]	Principal Cities [2]	Population	Physicians Under 65	Persons per Physician	Persons per Telephone [3]
Antelope		10,586	4	2,647	9
Brown		4,898	2	2,449	8
Buffalo		23,074	7	3,296	8
	Kearney	9,643			
Cass		15,034	6	2,506	7
	Plattsmouth	4,268			
Cedar		13,326	6	2,221	7
Dixon		9,023	3	3,008	5
Howard		7,016	2	3,508	12
Sarpy		11,417	3	3,806	17
Scotts Bluff		32,050	20	1,603	13
	Scotts Bluff	12,057			
	Gering	3,104			
York		12,756	4	3,189	5
	York	5,383			

1. Bureau of Census, estimated population 1943.
2. Bureau of Census, population 1940.
3. Based on 1940 figures, American Telephone and Telegraph Company.

A current knowledge of needs of communities for doctors is essential if adequate help is to be given veteran medical officers in their problems of medical practice. These needs can be indicated on the summary sheets under "Remarks" by the state and county secretaries and are then available to inquiring medical officers. Frequent reports from state and county medical societies about needs of communities for doctors will help maintain current files and will increase the service of the Bureau.

With the information available on a completely filled out summary sheet, it is readily possible for an interested medical officer to make an initial selection of areas in which he might like to practice. Since vacancies are held open in many communities for doctors now in military service, further investigation by direct correspondence with state and county medical societies will always be necessary to insure an accurate report of the needs of individual communities.

Council on Medical Service and Public Relations

PREPAID MEDICAL CARE

Medical Service and Indemnity Plans Sponsored by County and State Medical Societies

Consistent increase in membership marks the medical insurance plans sponsored by county and state medical organizations. This is the outstanding conclusion of the preliminary survey of many of these plans which has just been completed by the Council on Medical Service and Public Relations of the American Medical Association. Without exception the number of persons covered by these plans has shown a substantial increase within the last year; for example, Colorado 300 per cent, Wilmington, Del., 250 per cent, Massachusetts 400 per cent, Milwaukee 1,200 per cent, Kansas City 300 per cent, two New York plans 100 per cent. The Toledo, Ohio, plan has jumped from nothing a year ago to 43,273 subscribers now.

A study made by the Bureau of Economics of the American Medical Association in 1937, showing the growth in membership for thirty-five Blue Cross hospitalization plans between January 1936 and 1937, represents an increase in membership of 138 per cent during the twelve months. The number of members increased more than 200 per cent for the ten largest plans. For one plan the increase was 700 per cent. Although these voluntary medical plans have come into nationwide prominence only recently, the study shows that the movement has gained tremendous momentum during the last year and the figures compare favorably with those of the longer established Blue Cross plans of hospital insurance, when compared with the corresponding years of early operation. When the study of group hospitalization plans was made in 1937 the total membership was 700,000, the three largest plans having 49 per cent of all members. At the present time Blue Cross plans cover some twenty million people.

This present preliminary study on medical insurance programs indicates that a growth can be expected for these medical plans within the next eight years similar to that which marked Blue Cross from 1937 to 1945.

The first medical plan is believed to have been started in 1917 in Pierce County in the state of Washington. Little progress was made during the next decade. A rapid increase in number and size of these organizations was made during 1933-1940, when most of the county bureaus in the state of Washington were established. The most rapid growth has come since 1939, when statewide plans were started in Michigan and California.

In addition to plans now in operation, enabling legislation has been passed in several states in anticipation of the establishment of medical service plans. Active studies are now under way in Connecticut, Indiana, Illinois and several other states which should result in the early establishment of additional voluntary prepayment plans under the direction of or with the approval of state medical organizations. According to the information collected, the largest plan now in operation in point of membership is the Michigan Medical Service, which on May 31, 1945 had 777,104 subscribers.

The table on the following pages shows the wide variety of coverage. Also evident is the fact that the legal authority for the creation of the different plans varies greatly from state to state. Additional studies of these plans and other voluntary insurance plans will be made from time to time by the Council and the results published in THE JOURNAL.

Medical Service Plans

Name and Address	Year Organized	Number of Members Now	Number of Members Year Ago	Principal Benefits Provided	Charge	Annual Income
California Physicians' Service, 153 Kearny Street, San Francisco 8, or 743 South Grand View Street, Los Angeles 5	1939	102,000	102,000	(1) Surgery and hospitalization, employees and dependents alike (2) Medical, surgical and hospitalization for employees only	Employee, male, $1.45 female, 2.00 Employee and 1 dep., $3.80 Employee and 2 or more dep., $5.40 Medical rider (emp. only), $0.90	$2,300,000
Colorado Medical Service, Inc., 810 Fourteenth Street, Denver	1942	81,234	25,417	(1) Surgical care in doctor's office or hospital (2) Treatment of fractures and dislocations (3) Obstetric care (4) Lab. and x-ray up to $15 each per subscriber	Ind..... $0.75 mo. Family..... 2.00 mo. 2 persons..... 1.50 mo.	$460,835.28
Community Surgical Plan, 228 Superior Street, Toledo, Ohio	July 1944	43,276	None	(1) Surgical, obstetric (hospital, office, home) (2) X-ray (3) Anesthesia (4) Medical, in hospital for 70 days	(1) Ind..... $0.60 (2) Man and wife..... 1.50 (3) Family..... 2.00 (4) Additional rates quoted for each	$180,628
Dallas County Medical Plan, 433 Medical Arts Building, Dallas, Tex.	1940	1,444	366	(1) Medical care (2) Surgical care (3) Consultation services (4) X-ray, lab. and anesthesia (5) Obstetric services	Ind..... $1.75 mo.	$9,109.75
Group Hospital Service, Inc., 902 Orange Street, Wilmington, Del.	1943	56,341	19,021	(1) Surgical care (2) Anesthesia (3) X-ray (4) Obstetrics (5) Fractures	Ind..... $0.60 mo. Family..... 1.65 mo.	$153,753.45
Hawaii Medical Service Association, Hawaiian Trust Building, Hawaiian Trust Building, Room 417, Honolulu 48, T. H.	1938	9,272	7,507	(1) Medical care for 30 days (hospital) (2) Surgical care (3) X-ray and physical therapy (4) 6 office or home visits	Individual and dependents varies with monthly salary	$166,152.95
Hospital Care Association, Inc., 107 Market Street, Durham, N. C.	1933	Hosp. 67,780 H.&S. 41,784 111,564	72,792 23,627 96,419	(1) Hospital care (2) Surgical care	Ind..... $0.60 Family..... 1.60	$749,839.90
Hospital Saving Association of N. C., Inc., 165 E. Franklin St. Chapel Hill, N. C.	1935	Hosp., 161,695 H&S, 84,705 246,400	177,318 47,171 224,489	(1) Medical care (2) Surgical care	Ind. Family Hosp..... $0.60 $1.60 H. and S.... 1.20 2.50	$1,114,106.48
Iowa Medical Service, 222 Insurance Exchange Bldg., Des Moines Iowa	July 1945	Enrollment began July 1945	No experience	(1) Medical (2) Surgical (3) Obstetric (4) X-ray (5) Anesthesia	Med. & Surg. Surgical Ind..... $1.25 $1.00 Family..... 3.25 2.50	No experience
Massachusetts Medical Service, 280 Congress St., Boston	1942	124,676	29,295	(1) Surgical services (2) Anesthesia (3) X-ray (4) Endoscopy (5) Fractures (6) Obstetrics	Ind..... $0.85 mo. Husband and wife..... 1.65 Family..... 2.00	$288,227.99
Medical Service Association, Inc., 107 Market St., Durham, N. C.	1940	Regular 10,973 F. S. A. 30,284	Regular 12,388 F. S. A. 0	(1) Medical care } with F. S. A. members being covered only for surgical care (2) Surgical care }	Ind. male.....33 c. wk. Ind. female.....37. c. wk. Two persons....55 c. wk. Family.....65 c. wk. F.S.A. family $8.00	Total, $75,000 Reg., 53,000 F.S.A., 21,516 (11 mo.)
Medical Service Association of Pa., 222 Locust Street, Harrisburg, Pa.	1939	14,788	11,351	(1) Surgical care (2) Obstetric care (3) Treatment of fractures and dislocations in hospital	Ind..... $0.50 to $0.80 Dep..... 1.25 Family..... 2.00	$80,522.16
Medical and Surgical Care, Inc., 5 Hopper Street, Utica, N. Y.	1939	36,321	24,941	(1) Surgery and maternity (2) Anesthesia (3) X-rays (4) Metabolism (5) Cardiogram (6) Spec. lab. in hospital (7) Medical calls in hosp. plus 3 after	Plan 2 Plan 3 Ind..... $0.75 $0.48 Dep..... 0.75 0.51 Family..... 1.90 1.38	$248,265
Medical-Surgical Plan of New Jersey, 31 Clinton Street, Newark 2, New Jersey	1942	6/30/45 41,732	6/30/44 23,846	(1) Medical (2) Surgical (3) Obstetric (4) Anesthesia (5) Consulting } rendered in hospital (6) First aid surgery, rendered anywhere	Individual..... $0.75 Family..... 2.00	Year ending 6/30/45 $256,305.07
Michigan Medical Service, 1300 Washington Blvd. Bldg., Detroit 26	1939	777,104	622,997	(1) Surgical (2) Obstetric (3) Diagnostic x-ray not in excess of $15 each year (4) Anesthesia (5) Emergency surgical service	Ind., 60 c. to 90 c. per month subscription fees Two persons..... $1.60 Family..... 2.25	$1,918,921.56 Misc. income $17,993.90

Medical Service Plans

Annual Expenditure	Surplus and Reserve	Income Ceiling	Annual Benefit Limit	Legal Authority	Date Figures Based	Comment
$2,100,000.00	.....	$3,000.00	One year's care	Attorney General of state of California	6/14/45	Increased rates to beneficiary members, 30%. No surplus or reserve at present, but new rate increase will give surplus of about $200,000 by Dec. 31, 1945. 90% of membership notified of rate increase—acceptance by them with cancellation rate of less than one half of 1 per cent of membership
$231,211.00	$14,699.27	Ind., $1,500 per yr. 2 persons, $1,920 Families, $2,400	None	Incorporated under Colorado law governing nonprofit corporations in state. No enabling act	1945	
$102,628	Reserves Maternity $27,094 Unfiled claims, $10,837	None	None	State insurance laws	1944	June 23, 1945. Only one waiting period on maternity. No exclusion
$8,102.51	$10,061.22	Single, $2,500 Married, $3,000	$325.00	Charter granted by state of Texas	1944	
$93,557.23	$45,863.76	None	$150.00	None	1944	
$86,122.93	$106,192.45	$6,000		Charter given by the Territory of Hawaii for nonprofit organizations	5/31/45	The Kauai Medical Service Association has just been inaugurated on the island of Kauai—enrolment now under way. The plan is supported by the business firms and other local groups
$697,159.95	$190,000.00	None	None	Sp. enabling act, 1941 amended 1943	1944, financial 5/30/45, membership	
$1,003,447.24	$442,914.48	None	.....	Special enabling act, 1941. Amended in 1943 to include professional fee	1944	
No experience	No experience	$1,500 per year for individual; $2,500 family full service	21 days hospital and medical care per year	Code of Iowa, senate file 128	7/1/45	Plan is just now ready to enroll subscribers. Participating physicians are being enrolled at the present time
$197,365.01	$127,908.34	Participating physicians may charge extra only when patient's income exceeds $2,500 per year if married; $2,000 if single	No limit to number of admissions	Special act state legislature	1944	Includes $25,000 of surplus donated by Massachusetts Medical Society, refundable only when total surplus exceeds $225,000
90% actual amount available expenditure	10% maintained for operating expense	None	No limit	.....	12/3/44, financial 6/30/45, membership	
$70,242.20	$35,802.75	$3,120 (annually)	None	Enabling legislation, act of general assembly, 167, 168, 398, 399	4/30/45, enrollment 12/31/44, financial	
$174,772	$89,804.08	None	Plan 2 $225 Plan 3 $200	New York state	4/30/45	32% of Blue Cross Hospital Plan, Inc., members are all enrolled
7/1/44-6/30/45 $222,469.91*	6/30/45 $64,081.81	None for enrolment. Full service benefits to single contract $2,000; family $2,000 plus $500 for wife and $250 each child	21 days medical care; no limit for surgical	Special enabling act 1940 amended 1944, Rev. Stat. N. J.	6/30/45	Organized by Medical Society of N. J. Cooperates with Hospital Service Plan of N. J. In addition a separate organization (Medical Service Adm. of N. J.) operated state wide F. S. A. Plan and City of Newark Plan for indigent.
Services rendered $3,875,593.21 administration expense $574,063.39	$399,941.37	None (participating doctors may make additional charge) according to income	None, except for $15 for diagnostic x-rays	Michigan public act No. 109, 1939	5/31/45	

Medical Service Plans—Continued

Name and Address	Year Organized	Number of Members Now	Number of Members Year Ago	Principal Benefits Provided	Charge	Annual Income
Nebraska Surgical Plan, 330 City National Bank Bldg., Omaha, Neb.	1944	2,300	None	(1) Surgical operations (hospital or office) (2) Obstetric care (3) Limited x-ray examinations	Ind. $0.75 Dep. 1.50 Family 2.00	
New Hampshire Physician Service, 89 N. Main Street, Concord, N. H.	1944	(12/31/44) 4,881	(not organized) None	(1) Surgical service, limit $150 (2) Anesthesia, lab. and x-ray exam. (3) Maternity (4) Medical service, 25 doctor's visits	Ind. (co. service) $0.75 Two persons 1.50 Family 1.75	$5,117.63
Oregon Physicians' Service, 471 Pittock Block, Portland 5, Ore.	1941	90,000	82,000	(1) Complete medical for services ... employee (2) Complete hospital group services	Ind., $2.50 per mo. or $0.60 per wk. Dependents, no coverage Family, no coverage	$2,400,000.00
Surgical Care, 208 E. Wisconsin Avenue, Milwaukee	1943	(1/1/45) 3,519	(1/1/44) 266	(1) Surgical services (2) Obstetric services on family contract (3) Medical services	Ind., 90 c. per mo. One dependent, $1.75 (without obstetrics) Family, $2.50 (ob. included	$16,003.85
Surgical Care, Inc., 531Argyle Building, Kansas City 6, Mo.	1943	40,000	13,000	(1) Surgery (2) Obstetrics (3) Orthopedics (4) Anesthesia (5) X-ray (6) Radiation therapy	Ind., $0.75 per mo. mbr. and 1 dep., $1.50 Family, $2 (mbr. and 1 dep., maternity benefits included, $2)	$200,000.00
United Medical Service, Inc., 370 Lexington Ave., New York 17	1944	79,494	37,561	Contract: (1) Medical, (2) Surgical, (3) Obstetric Indemnity ... Ind. $0.40, Hus. & Wife $1.00, Family $1.80 Surgical service ... 0.52, 1.12, 2.00 Surgical and medical ... 0.64, 1.36, 2.36		$324,467.43
Washington State Medical Bureau, 218 Cobb Building, Seattle, Wash.	....	250,000	.....	(1) Medical (2) Hospital, ambulance (3) Dental and nursing care	Premiums run from $1.75 to $2.75 and up to $7.75 for full family coverage	$500,000 per mo. or about $6,000,000 per yr.
Western New York Medical Plan, Inc., 888 Delaware Avenue, Buffalo	1940	3/30/45 45,000	3/30/44 24,171	(1) Surgical (2) 25 house, office or hosp. calls (3) Anesthesia (4) $5 specialist x-ray consultation (5) $5 specialist endoscopic exam. (6) Maternity care	Surg. Med. Surg. Ind. $0.60 $1.50 Dep. .... Family 1.70 3.00 (per month)	$280,314.17

LOUIS H. PINK TO REORGANIZE INSURANCE INDUSTRY IN PHILIPPINES

Louis H. Pink, president of Associated Hospital Service of New York and former superintendent of insurance of the state of New York, is en route for Manila, where he will serve temporarily as special adviser to the Philippine government in the reorganization of the insurance industry of the islands, it was announced on June 18 by Jamie Hernandez, secretary of finance of the Philippines. Mr. Pink accepted the Philippine post in response to a personal appeal from President Sergio Osmena.

Leonard M. Gardner of Portland, Ore., who is accompanying Mr. Pink as associate adviser, will remain in the islands for an indefinite period to assist the Philippine government in carrying out the program of reorganization.

The resolution of the board of directors of Associated Hospital Service of New York granting Mr. Pink leave of absence until September to serve the Philippine government is in keeping with the organization's policy of cooperation in public service activities.

INCORPORATORS OF CONNECTICUT MEDICAL SERVICE

Six members of the Connecuticut State Medical Society have been named incorporators of the Connecticut Medical Service, the prepayment plan which is soon to be launched in the state. The society's representatives are Edmund L. Douglass, Groton; Ira V. Hiscock, professor of public health, Yale University School of Medicine; H. Goldersleeve Jarvis, Hartford; James Raglan Miller, Hartford; J. Harold Root, Waterbury, and Charles H. Sprague, Bridgeport. Five laymen active in civic affairs, particularly in the health and welfare field, are the remaining members of the board: Dr. D. Spencer Berger, treasurer, Berger Brothers, New Haven; Wallace E. Campbell, secretary, Fuller Brush Company, Hartford; J. William Hope, president, J. William Hope Company, accountants, Bridgeport; Robert S. Judd, vice president, Southern New England Telephone Company, New Haven; Edward J. Quinlan, judge of the superior court, Norwalk.

WARNER EXPANDS GROUP INSURANCE PROGRAM

A liberal expansion in the group insurance program of William R. Warner & Co., Inc., and its subsidiary companies, Richard Hudnut and Standard Laboratories, Inc., was made effective May 1 according to an announcement by John H. Holzbog, vice president in charge of industrial relations. In addition to the life insurance program which the company had previously carried for its employees, the new plan includes accidental death and dismemberment coverage, weekly sickness and accident benefits, surgical benefits, daily hospital benefits of $5 a day for employees and dependents, and an additional allowance for special hospital charges of five times the daily hospital benefit, which also extends to employees and their dependents. Employees who have been with the company for three months or more are eligible for the full coverage. The plan will include employees of the company's plants in New York, St. Louis and Mamaroneck as well as all salesmen and field representatives in the United States. Approval has also been sought from the Canadian War Labor Board for including employees of the company in Canada. The entire cost of the program is being carried by the company.

The plan is being underwritten by the Travelers Insurance Company of America.

Medical Service Plans—Continued

Annual Expenditure	Surplus and Reserve	Income Ceiling	Annual Benefit Limit	Legal Authority	Date Figures Based	Comment
Less than 1 yr. in operation	$10,000	None	Limited to $250 maximum for each person on agreement	State of Nebraska under assessment insurance law	6/30/45	Organization only in operation 8 months
$9,449.07	$4,331.44	None	None	State law	8/1/44 to 12/31/44	
$2,400,000.00	$75,000.00	None	One year's total service and 6 months hospital service for any single ailment	License from Oregon State Insurance Dept.	5/1/45	No definite income ceiling set but coverage of high income people avoided wherever possible
$13,057.80	$3,546.65	Single person, $1,800 married person, combined income of $2,400 plus additional allowance of $200 per dependent	None	Corporate charter of the Medical Society of Milwaukee County	1/1/43 to 1/1/45	
$170,000.00	$44,500.00	None	None	No enabling act; Pro forma corporation under religious, benevolent and educational statutes	5/31/45	
$ 225,016.67	$187,857.58	None for purchase of coverage	None	Article ix-c of New York state insurance law	12/31/44	Service benefits under "service" contracts available for single persons with annual incomes of $1,800 or less and married persons with annual incomes of $2,500 or less; subscribers with incomes above these amounts receive indemnity benefits only
.....	None	Income ceiling discarded except in couple of bureaus where it is $3,600	Benefits limited to from six months to one year's time	Washington State Medical Association and Washington Physicians Service, Inc. (The latter on insurance company to comply with state insurance code)	7/17/45	Pierce county, first bureau organized in 1917. Bulk of other 16 bureaus established in 1933-1935. Organization still going on, with three or four now in process of being established. Medical and hospital plans are being developed for families of workers covered; already in force in some bureaus
$242,798.56	$11,458.63	None	None	Article ix-c N. Y. State Ins. law	12/31/44	

Medical Economic Abstracts

MEDICAL SERVICE PLANS IN CONTINENTAL COUNTRIES

This is the first of a series of abstracts on medical service plans in foreign countries which will appear in THE JOURNAL from time to time, prepared by the Council on Medical Service and Public Relations. The following was taken from the *British Medical Journal:*

Denmark

Denmark's peculiar contribution to social legislation lies in the field of social insurance. The state organizes and regulates insurance and in part runs the insurance administration itself. National insurance covers the entire population. Previous to what is known as the Social Reform—a mass of social legislation which was passed in 1933—there was a voluntary system of sick clubs or sickness benefit societies which covered about two thirds of the population, and this has been preserved within the national compulsory system. Every person on reaching 21 is required to become a member either of a sick club or of a state-controlled sickness insurance institution. In the sick club there are two classes of members. The "active members" consist of those who are "unpropertied"; that is, with an annual income of less than about 3,500 kroner (just under £200). The second class, the "passive members," consist of those who are above the income level and are not eligible for the benefits of the club, but should their income fall below the stated level they may, irrespective of their state of health, on complying with the conditions become "active members."

In illness the sick club provides its "active members" with entirely or partly free domiciliary medical attendance, free treatment at a hospital (where the municipality meets half the expense), two thirds of the expenditure on medicines and cash benefit up to twenty-six weeks. Special maternity benefits have been introduced.

There are 1,650 sick clubs, all separate units but all subject to state supervision. Of their total income about 68 per cent comes from members' contributions and 28 per cent from state and communal grants. The real significance of the general obligation brought about by the National Insurance Act to be a member either of a sick club or of a national insurance institution lies in the fact that the act also introduced a general and compulsory invalidity insurance the premium for which is collected with the sick club contribution, and also that no one can obtain the old age pension without being a member. Thus the provision of help in sickness, in invalidity and in old age is joined together in a common insurance system.

Under social insurance medical service is provided by practitioners working under agreements. The agreements are divided into two different categories. Outside Copenhagen the insurance institutions have no authority to select practitioners; all physicians who report to the regional section of the Danish Medical Association that they are willing to serve may be placed on the list. In Copenhagen, on the other hand, the doctors are engaged by the insurance institutions. Nearly all medical practitioners in Denmark, except the specialists, engage in insurance practice. Doctors may be remunerated either by a capitation fee or according to a schedule of fees for the services they render. The amount paid for medical services is divided about equally between these two forms of arrangement.

Considerable choice of doctor is allowed to the patient in Copenhagen, though not complete free choice. The city is divided into three main districts, and insured persons may make their choice among the local contracting physicians in their district. However, no physician may accept more than 1,500 persons as potential patients, and consequently this limits free choice.

Washington Letter

(From a Special Correspondent)

Aug. 13, 1945.

Hawley Reported to Be New Medical Chief of Veterans Administration

The new medical director of the Veterans Administration is expected to be Major Gen. Paul Hawley of the Army Medical Corps, who since January 1943 has been chief surgeon of the Army in the European theater. General Bradley, new Veterans Administrator, who worked with General Hawley, is expected to announce the appointment when he takes over as Veterans chief this week. The job was reported to have been lined up previously for Col. Howard A. Rusk of the Army Air Forces, who conferred with President Truman and General Bradley on a rehabilitation program for war veterans. General Hawley is a native of Indiana and a graduate of the University of Cincinnati Medical School.

Request for Four State Pollution Survey of the Potomac River

The U. S. Public Health Service has been asked by the newly organized Interstate Commission for the Potomac River Basin to make a pollution survey of the 14,500 square mile drainage area in four states, according to an announcement from Hershey, Pa. The commission, pending receipt of the requested data, has tentatively divided the basin into three water use classification. It recommends treatment of all water taken from the Potomac and its tributaries. The commission includes representatives of Pennsylvania, Maryland, Virginia, West Virginia, the District of Columbia and the federal government. It has classified as unfit for either drinking or swimming the waters of the Potomac in Metropolitan Washington, the Luke-Cumberland area and the north branch to Patterson creek, described as the worst polluted sections of the basin.

UNNRA to Combat Yellow Fever Throughout the World

Dr. Fabio Carmeiro de Mendonca, Brazilian physician and director of quarantine for Brazil, who arrived here from Rio de Janeiro recently, states that "UNNRA will shortly inaugurate a world campaign for the eradication of yellow fever. It will be one of its major projects in disease prevention. The yearly death toll from this disease is considerable. It is quite prevalent in the islands of the Pacific. Brazil is no longer menaced with yellow fever as it is known in the United States. We do have some infectious diseases similar to yellow fever." Dr. Mendonca conferred here with prominent U. S. medical authorities on preventive measures for yellow fever.

Improvement of German Health and Sanitation in United States Zone

Steady improvement in restoration of German health and sanitation, economy and local civil government is reported in the U. S. zone of occupation by the War Department. The report said that health conditions are gradually being bettered. Typhus has decreased. Tuberculosis and venereal disease have been serious among displaced persons. Typhoid, dysentery, diphtheria and scarlet fever cases are being reduced. Food continues to be a primary concern, with Allied displaced persons receiving, through priorities, daily diets of 2,000 calories. Water services have been restored for drinking water at least. Selected industries are making critical items such as soap, fertilizer, insecticide and processed food.

Development of Improved Artificial Hand by Navy Technicians

An improved artificial hand made of plastic materials, which is said to be natural looking and far superior in use and appearance to anything previously devised, is revealed as the work of dentists and enlisted men working under Capt. Rae D. Pitton and Lieut. Comdr. LeMar W. Harris, former Chicago dentist, at the Naval Dental School, Bethesda, Md. Dr. Harris got his start in plastics making artificial teeth. Following research extending over more than a year, they are said to have produced a hand that looks real, doesn't require wearing a glove, is almost as efficient as a hook, picks up and holds articles in a rubber-like grip and weighs less than a pound. While some amputees will get the new hand soon, mass production is not expected for some time. The prosthetic appliance is made of a special plastic and is tinted to match the patient's skin. A 1 pound cam mechanism hidden inside the hand is said to permit natural finger movement. The mechanism is operated by a cord running up the arm and around the shoulders. Control is by the shoulder muscles. The new hand is the first improvement in artificial limbs to be announced since the government's appeal for new ideas.

Standardized Form of Treatment for Poliomyelitis Predicted

Standardization of treatment for infantile paralysis is predicted by District of Columbia medical men. They expect that medical research now under way will combine the best features of the Kenny and other treatments to develop the most effective system. Dr. P. A. McLendon, chairman of the Children's Hospital poliomyelitis committee, reports that types of treatment differ with individual physicians. Some methods are successful in some cases and failures in others. As an illustration, ultraviolet irradiation, drawing out blood and bathing it with violet rays helps to combat infection in bulbar poliomyelitis, but it does not help spinal paralysis cases. The Kenny hot pack and manipulation method was said to have both advantages and disadvantages. While this treatment helps some patients, the extreme heat is believed to be detrimental to the patient's health.

Capital Notes

In a rabies control program, District of Columbia medical authorities have announced that 35,000 dogs will be vaccinated by September 7 at ten strategically located clinics.

District school teachers are studying improved health education methods at daily conferences in Wilson Teachers College. Speakers include Dr. Irma Nevins, national director of accident prevention, Red Cross; Frank S. Stafford, chief of health education, U. S. Office of Education, and Miss Bosse Randle, special consultant, school health services, Children's Bureau.

Russell Green, a University of Maryland sophomore whose left side was paralyzed when he was 10, is demonstrating to disabled veterans in Walter Reed Hospital how he learned to walk, dance, swim, type with one hand and tie his shoes.

Dr. Paul F. Douglask, president of American University, has announced plans for a $2,000,000 six story center of social science and public affairs.

Woman's Auxiliary

West Virginia

Dr. W. W. Bauer, director of Health Education of the American Medical Association, and Dr. Harry V. Thomas, president of the Harrison County Medical Society, were the guest speakers of the Harrison County Auxiliary Doctor's Day Program.

The Raleigh County Woman's Auxiliary recently announced the establishment of a "Book Shelf" at the Pinehill Sanitarium.

Mrs. U. G. McClure, president of the Woman's Auxiliary to the West Virginia State Medical Association, recently announced the appointment of a Physicians Advisory Board for 1945-46, as follows: Drs. Hu C. Myers, Philippi; H. V. Thomas, Clarksburg; John P. Helmick, Fairmont; Scott A. Ford, Beckley, and U. G. McClure, Charleston. The following chairmen of standing committees have been appointed by Mrs. McClure to serve with other chairmen named late in May: convention, Mrs. Edwin J. Humphrey, Huntington; press and publicity, Mrs. W. Paul Elkin, Charleston, and speakers' bureau, Mrs. John W. Hash, Charleston.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Faculty Changes.—Frederick E. Emery, Ph.D., associate professor of physiology, University of Buffalo School of Medicine, Buffalo, N. Y., has been appointed professor of physiology and head of the department of physiology and pharmacology of the University of Arkansas School of Medicine, Little Rock. John E. Davis, Ph.D., is professor of pharmacology in the department.

State Cancer Commission Created.—Under recent action of the legislature, a state cancer commission has been created to coordinate and direct a cancer control program in Arkansas to be financed by an initial appropriation of $25,000. The law providing for the commission stipulates that the funds may be used to furnish medical, hospital and home care for indigent cancer patients and may be matched with county and city funds in making available care for persons not wholly indigent. According to the *Field Army News* of the American Cancer Society, the commission may accept voluntary contributions and disburse any federal funds available for cancer control, conduct clinics wherever necessary in the state and institute educational programs in cooperation with established organizations as well as utilize facilities of private physicians and hospitals and the University of Arkansas School of Medicine. Gov. Ben Laney has been named chairman of the Arkansas State Cancer Commission and Dr. Carl A. Rosenbaum, associate professor of surgery at the medical school, secretary.

COLORADO

Anniversary Year of State Medical Society.—The Colorado State Medical Society this year will observe its seventy-fifth anniversary. Plans are under way to mark the occasion in some special manner.

New Professor of Pathology.—Dr. James Bernard McNaught, associate professor of pathology, Stanford University School of Medicine, San Francisco, has been appointed professor of pathology at the University of Colorado School of Medicine, Denver. Dr. McNaught graduated at Stanford in 1931.

Building Fund Revived.—On June 26 twenty past presidents of the Medical Society of the City and County of Denver gave a dinner to the members of the society to mark the revival of the dormant building fund campaign. Talks at the dinner revealed the status of homes owned by other societies and the facilities of other libraries as compared with the library facilities of the Denver society. A site has not been selected for the proposed permanent home of the society, the choice to be deferred until a majority of all members has voted its choice of location.

CONNECTICUT

Clinical Congress Canceled.—For the first time in twenty-six years the clinical congress of the Connecticut State Medical Society will not be held this fall.

Personal.—On June 1 Mr. Berger E. Foss, superintendent of the Knickerbocker Hospital, New York, became director of Newington Home for Crippled Children, a 200 bed orthopedic children's hospital, Newington, succeeding Miss Constance Leigh, R.N., who retired after twenty-seven years' service in that capacity.

ILLINOIS

Governor Vetoes Medical Bill.—The Allison bill, which was passed by the legislature and which would have made it unlawful for any physician or surgeon to refuse emergency or first aid treatment to an accident victim, was vetoed July 24 by Governor Green, according to the Chicago *Sun*.

Maude Etheredge Resigns at Illinois.—Dr. Maude Lee Etheredge, director of the women's health service and professor of hygiene, University of Illinois, Urbana, has resigned after twenty-two years' service to the university, according to the Urbana *Courier*, July 2. The resignation will be effective September 1. Dr. Etheredge graduated at Bennett College of Eclectic Medicine and Surgery, Chicago, in 1911. Prior to joining Illinois in 1923 she acted as medical adviser and was director of the women's health service at Cornell University, Ithaca, N. Y.

Chicago

Course in Bronchoesophagology.—The department of otolaryngology, University of Illinois College of Medicine, will offer a special course in bronchoesophagology, October 15-27, under the personal direction of Dr. Paul Holinger, assistant professor of laryngology, rhinology and otology. The course will consist of didactic lectures, animal and cadaver demonstrations, practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics and other work. Registration will be closed when the limited number of twelve applications of physicians have been received. Additional information may be obtained from the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12.

Emotional Adjustments of Civilians and Veterans.—The Illinois Society for Mental Hygiene is offering its services in the planning of educational programs to promote better understanding of the emotional adjustments of civilians and veterans. The service is available, without charge, to organizations wishing a list of speakers, a series of appropriate movies and a selection of literature for distribution or sale. Arrangements for hall, speakers, movies and audience will be left to the organization wishing the planning service. If the group wishes the Illinois Society for Mental Hygiene to conduct programs, a charge will be made for the cost price of the speakers' fees, movies and any other expense incurred. Additional information may be obtained from the Illinois Society for Mental Hygiene, 343 South Dearborn Street, Chicago 4.

KANSAS

Postgraduate Fund.—The Kansas Medical Society has voted to raise a fund of $100,000 to assist returning medical officers in obtaining postgraduate medical education before reentering private practice. A questionnaire has been sent to each member of the society now serving with the armed forces asking his plans for postgraduate education. Dr. William P. Callahan, president of the Kansas Medical Society, has appointed as a committee to study the distribution to be made of the fund of $100,000, more than $36,000 of which is now available, Drs. Harold H. Jones, Winfield, chairman; Floyd C. Beelman, Topeka; Clarence H. Benage, Pittsburg; Louis B. Gloyne, Kansas City; John L. Lattimore, Topeka; Benjamin H. Mayer, Ellsworth, and James H. A. Peck, St. Francis. It has already been decided that each medical officer desiring postgraduate medical education shall have the opportunity of receiving assistance from the fund and that each shall select the school and the course of study he prefers. The *Journal of the Kansas Medical Society* states that contributions to the fund are voluntary but that it is hoped each member will send in a donation.

KENTUCKY

Hugh Leavell Joins Rockefeller Foundation.—Dr. Hugh R. Leavell, Louisville, director of the Jefferson County Board of Health, who has been on leave with the UNRRA in Europe, has been appointed an assistant director for the medical sciences for the Rockefeller Foundation. The appointment will be effective in the fall, when his association with the UNRRA ends. Dr. Leavell has been connected with the Jefferson board of health since 1934.

MISSOURI

Personal.—Dr. Curtis H. Lohr, St. Louis, was to resume his activities June 15 as superintendent of the St. Louis County Hospital, Clayton, after a two year absence on overseas duty with the army.——Dr. William E. Angell, Rocheport, recently observed the fiftieth year in the practice of medicine.

The Doctor Prefix Bill.—House Bill 206, known as the "Doctor Prefix Bill," has been approved by the governor and will become law ninety days after the adjournment of the present session of the legislature, which is not expected until after January 1. To comply with the law, physicians should change their office name plates, cards, stationery, signs and so on by adding M.D. after the name whenever the word "Doctor" or "Dr." is used before the name. The law applies as well to dentists, osteopaths, veterinarians, chiropractors, chiropodists or any other persons who profess to be practicing the healing art and who use the prefix "Doctor" or "Dr."

Study of Tuberculous Pulmonary Calcification in Children.—The U. S. Public Health Service has established a laboratory at the University of Kansas School of Medicine, Kansas City, with a mycologist in charge to carry on a study of tuberculous pulmonary calcification. In cooperation of the local health department and the Kansas City Tuberculosis Society, the public health service is conducting a field study among the children, consisting of a tuberculosis and histoplasma skin test with an x-ray plate of the chest. The U. S. Public Health Service in 1944 investigated the question of pulmonary calcification in the absence of the tuberculin positive skin test, carrying on investigations in Detroit, Minneapolis, Philadelphia and Kansas City. Histoplasmin skin tests were made concurrently with tuberculin tests, and results suggest that much of the pulmonary calcification hitherto suspected of being tuberculosis is in reality due to a subclinical infection with Histoplasma capsulatum or an immunologically related organism.

NEBRASKA

Personal.—Dr. Charles W. Rudolph, Houston, Texas, has been appointed in charge of the Hospital for the Tuberculous, Kearney, succeeding Dr. Leland C. Albertson, resigned (THE JOURNAL, May 19, p. 216).

Hospital News.—Ground for the proposed 50 bed $270,000 Provident Hospital, Omaha, to be built by the Nebraska Negro Medical Society and other sponsoring groups, was bought July 9. The site is at Thirtieth and Wirt streets.

First Fellowship Under Poynter Foundation.—Philip D. McIntosh, B.S., who has completed his first two years of medicine in the University of Nebraska College of Medicine, Omaha, has been selected as the first C. W. M. Poynter Foundation Fellow in medical science for a period of a year beginning July 1 (THE JOURNAL, March 3, p. 534).

NEW JERSEY

"Polio" Quarantine in Trenton.—On August 5 a poliomyelitis quarantine became effective in Trenton, barring children under 16 years of age from churches, Sunday schools, theaters, stores, playgrounds, parks and gatherings of any kind. A resolution imposing the quarantine and fixing penalties for parents or others permitting violations by children was adopted by the city commission on August 4. Two days previously Dr. William E. Mountford, city health officer, asked the commission to act, and when it failed to do so he asked the public to comply voluntarily with his proposal. According to the New York *Times*, the number of poliomyelitis cases on August 4 totaled 45, with eight deaths.

NEW YORK

Memorial Library to Honor Physician.—Members of the medical staff of the Mount Vernon Hospital, Mount Vernon, and of the Mount Vernon Medical Society, as well as personal friends, are cooperating in the establishment of a library at the Mount Vernon Hospital to be named the Dr. Ludwig B. Goldhorn Memorial Library. The library will honor Dr. Goldhorn, who died Nov. 16, 1944 after serving the hospital for thirty-six years as roentgenologist, during which he established the first x-ray laboratories there.

Cancer Teaching Day.—On October 17 a cancer teaching day will be held at the Governor Clinton Hotel, Kingston, under the auspices of the Medical Society of the County of Ulster, the Third District Branch of the state medical society, the Tumor Clinic Association of the State of New York, the medical society and the state department of health's division of cancer control. Speakers will include:

Dr. Earl D. Osborne, Buffalo, Cancer of the Skin and Allied Tumors.
Dr. Frederick S. Wetherell, Syracuse, Role of the Practicing Physician in the Care of Cancer.
Dr. Charles B. Huggins, Chicago, Cancer of the Prostate.
Dr. Fred W. Stewart, New York, Biopsy in Tumors.

Agencies Named for Hospital Survey.—To make the proposed new hospitals in the state eligible for federal funds under the pending Hill-Burton hospital construction bill, Governor Dewey on August 2 designated the Postwar Planning Commission as the single state agency for surveys as required in section 612 (a) (1) of the bill and set up a Joint Hospital Board composed of the commissioners of health, mental hygiene and social welfare to coordinate activities in these fields which are required in the survey. The Joint Hospital Board will act for and with the planning commission in making the necessary inventory and survey of hospitals in the state. Needed experts are to be employed with funds furnished by the Postwar Planning Commission. The state advisory council required in section 612 (a) (2) of the Hill-Burton bill will be designated by the Joint Hospital Board.

New York City

Course in Hospital Administration.—Columbia University announces that, aided by a grant from the W. K. Kellogg Foundation, it will offer a course in hospital administration beginning September 27. The course will be of approximately twenty-one months' duration, consisting of an academic year in residence and a calendar year of supervised assistantship in an affiliated hospital. A baccalaureate degree will be a minimum requirement. Women will be admitted on the same terms as men. The course will be offered through the School of Public Health of the faculty of medicine of the university, according to an announcement.

Changes at Columbia.—Drs. James Wesley Jobling and Alwin Max Pappenheimer, professors of pathology at Columbia University College of Physicians and Surgeons, have been designated professors emeritus, the New York *Times* of July 26 reports. Dr. Jobling, who graduated at Lincoln Memorial University Medical Department, Knoxville, Tenn., in 1896, has been associated with Columbia since 1918. Dr. Pappenheimer, who graduated at Columbia in 1902, has been associated there since 1909. Aura E. Severinghaus, Ph.D., and Dr. Vernon W. Lippard are associate deans for medicine at Columbia. Dr. Harry S. Mustard, director of the DeLamar Institute of Public Health, is associate dean for public health.

Progress of Plans for Tropical Disease Hospital.—On July 16 federal approval was given to an advance of $76,000 to the city of New York to help finance the preparation of plans of a $2,200,000 hospital for tropical and communicable diseases to be constructed after the war. The federal advance, made through the bureau of community facilities, FWA, will be supplemented by $19,000 authorized by the board of estimate. The hospital will have a capacity of 300 patients. It is to be built on a tract facing the Hudson River, between 165th and 168th streets, and transferred to the city by agreement with Columbia University and the Presbyterian Hospital of the City of New York. On the same tract, a short distance north of the hospital, the city proposes to build a $2,690,000 public health laboratory, research and training center (THE JOURNAL, June 9, p. 453).

WASHINGTON

New Rule Relating to Medical Treatment.—The state department of labor and industries has reported to the Washington State Medical Association the adoption of a new rule relating to medical treatment, effective June 7. The rule stipulates that in any case in which the original report and diagnosis of the attending physician is used as a basis for the rejection of the claim, the physician shall be entitled to payment for his services on the first call, including x-rays and laboratory work necessitated for diagnostic purposes, in accordance with the fees prescribed in the fee schedule. In the past, when the department found it necessary to reject a claim on the basis that the condition present was not the result of an injury, and that action was based on the report of the attending physician, the physician's bill was also rejected. In other words, he was penalized for reporting the exact facts. The new rule will overcome that situation.

WEST VIRGINIA

Physicians Urge Extension of Current Medical Care.—The expansion of existing nonprofit medical and hospital service plans and the development of new plans to make medical and hospital care available to people residing in every part of West Virginia was recommended to the legislative interim committee by eight medical members of the recently appointed advisory committee (THE JOURNAL, June 23, p. 606). The plan was recommended in preference to a statewide plan. At the present time there are ten hospital service plans and nine medical service plans in operation in this state. The committee recommended that service corporations be developed and operated separately and that hospital care be made the responsibility of participating hospitals and medical service the responsibility of participating physicians. In the interest of economy of operation, the committee feels that hospital service groups should be permitted to serve as public agents for medical service corporations in the same area. The committee also recommended that reciprocal relations be arranged by which a member of a service group in one area may receive hospital or medical service in any other area of the state where service plans are in operation. It is felt that service outside the state should be on an indemnity basis only, unless reciprocal arrangements can be made by the plans operating in West Virginia and those in operation in other states. Under the plan recom-

mended by the doctor group, all state employees would be eligible to participate on a voluntary basis in nonprofit medical and hospital service plans, with provisions for salary deductions at the source covering this service. The group unanimously recommended that a division of medical and hospital service be created in the state health department under the supervision of a director, who would have such regulatory powers over nonprofit service plans as may hereafter be defined. The director would have the assistance of an advisory committee appointed by the governor, composed of two representatives each from the West Virginia State Medical Association, the Hospital Association of West Virginia, nonprofit hospital service plans operating in West Virginia and the public. The committee urged that at least one third of the members of the directing board of the various nonprofit hospital and medical service plans should be representatives of the public at large; that is, persons who are not doctors and who have no hospital affiliations. The group declared that the funds provided at the present time for medical and hospital care for the indigent have proved to be wholly inadequate for the purpose and recommended that a substantial increase be made in the appropriation. The revised plan would provide for emergency hospital and medical service for the indigent on a twenty-four hour basis. Dr. Robert J. Wilkinson, Huntington, chairman of the medical members of the advisory committee, submitted the report for the group. He stated that the program as outlined is acceptable to all of the service plans now in operation in the state with the exception of the recommendation for supervisory and regulatory control by the director of a new division to be created in the state health department. Six of the service plans favor regulation by the insurance commissioner, while representatives of two of the plans favor the creation of a new division.

GENERAL

Ophthalmology Examination Postponed.—The American Board of Ophthalmology announces that because of transportation difficulties the examination of the board, originally scheduled for Chicago in October, has been postponed to Jan. 18-22, 1946. Examinations of the board will be Chicago January 18-22, Los Angeles January 28-February 1, New York in May or June and Chicago in October.

Antinoise Awards.—Memphis, Tenn., was named first prize winner of the Grand National award, a gold plaque, presented for the first time this year by the National Noise Abatement Council, New York. Winners of the 1945 four city population group awards, silver plaques, include group I (cities over 500,000), Chicago; group II (250,000 to 500,000), Rochester, N. Y.; group III (100,000 to 250,000), Salt Lake City, Utah; group IV (less than 100,000), Little Rock, Ark.

Publicity Program for Radiology.—The commission on public relations of the American College of Radiology has received a grant of $15,000 from the National Electrical Manufacturers' Association to conduct a publicity campaign in connection with the commemoration of the fiftieth anniversary of Roentgen's discovery of the x-rays. The campaign will be directed by a joint committee representing the college and the manufacturers' association. Through newspapers, periodicals and the radio, the role of the specialist in radiology as a doctor and consultant will be described. The campaign will end November 8, the fiftieth anniversary of Roentgen's discovery.

Ammonia.—The rapid growth of new chemicals and the widening industrial use of well known ones, especially during the war, has led the Division of Labor Standards in the U. S. Department of Labor to inaugurate a series of bulletins on controlling chemical hazards in cooperation with the Manufacturing Chemists Association of the United States, according to V. A. Zimmer, director. The first bulletin, "Ammonia," is just off the press and others shortly to be issued cover chlorine, sulfuric and nitric acids, formaldehyde and the anilines. There will be over a hundred such bulletins in the series. These bulletins are designed for safety men in industry, insurance companies and state labor departments, for union safety committees and for materials warehousemen, handlers on railroads and trucking concerns, industrial doctors and nurses and firemen and fire prevention authorities. Each bulletin describes the hazards of the chemical, its characteristics, safety precautions for installation, handling and storage, protective clothing, permissible and hazardous concentrations, and first aid treatment. A bibliography is included. Each bulletin is checked for technical accuracy and practical safeguards with firms manufacturing the chemical through the Manufacturing Chemists Association. "Ammonia" will be of special interest to refrigeration and air conditioning manufacturers, oil refineries, steel treatment and water purification plants, manufacturers of sulfuric and nitric acids, fertilizer, drugs and chemicals, and bottling works. A supply of up to twenty-five copies will be distributed without charge on request by the Division of Labor Standards as long as the free supply lasts. Larger orders may be obtained for 5 cents a copy from the Superintendent of Documents, Government Printing Office, Washington 25, D. C. A 25 per cent discount is allowed on orders of 100 or more.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the week ended August 4 have been received from the division of public health methods, U. S. Public Health Service, as follows:

Division and State	Poliomyelitis Week Ended 8/4, 1945	Poliomyelitis Week Ended 8/5, 1944
New England States:		
Maine	2	1
New Hampshire	2	1
Vermont	5	1
Massachusetts	15	23
Rhode Island	0	0
Connecticut	9	10
Middle Atlantic States:		
New York	83	311
New Jersey	82	16
Pennsylvania	31	86
East North Central States:		
Ohio	12	48
Indiana	5	36
Illinois	26	14
Michigan	5	40
Wisconsin	3	5
West North Central States:		
Minnesota	1	14
Iowa	5	1
Missouri	4	4
North Dakota	0	0
South Dakota	0	0
Nebraska	0	4
Kansas	5	5
South Atlantic States:		
Delaware	2	3
Maryland	6	27
District of Columbia	3	9
Virginia	15	63
West Virginia	0	7
North Carolina	6	40
South Carolina	8	4
Georgia	5	7
Florida	1	7
East South Central States:		
Kentucky	0	65
Tennessee	23	4
Alabama	4	5
Mississippi	1	10
West South Central States:		
Arkansas	2	0
Louisiana	4	21
Oklahoma	14	1
Texas	38	5
Mountain States:		
Montana	0	0
Idaho	0	0
Wyoming	0	0
Colorado	5	0
New Mexico	1	2
Arizona	0	1
Utah	12	1
Nevada	0	0
Pacific States:		
Washington	12	5
Oregon	1	16
California	18	9
Total	476	932
First 31 weeks:		
1945 and 1944	2,915	3,992
Median, 1940-1944	1,852	

Four Million Dollars for Cancer Research.—The Alfred P. Sloan Foundation has given $4,000,000 to provide and in part to maintain a proposed Sloan-Kettering Institute for Cancer Research, to be organized in conjunction with Memorial Hospital for Cancer and Allied Diseases, New York. The gift will provide for a building especially designed for the purpose and self contained in all its various research functions. It will be erected at an estimated cost of $2,000,000 on property now owned by Memorial Hospital adjacent to its present location. The facilities to be provided will be adequate to permit the exploration of all avenues that may be expected to contribute to the objective. The entire project will be in keeping with a program of expansion at Memorial Hospital. In addition, the Alfred P. Sloan Foundation will undertake to provide $200,000 a year toward the operating cost for a definite period of ten years. In a statement to the press, Reginald G. Coombe, president of the hospital, said that, while the Alfred P. Sloan Foundation gift provides for most of the financial requirements of the research phase of the proposed Memorial Cancer Center, the center will not be fully effective from the point of view of its ability to render service until it is completed. It is planned to launch a public campaign to obtain the necessary $3,000,000 to $4,000,000 to provide for an increased bed capacity at Memorial Hospital proper, for fellowships for the training of specialized medical personnel and for equipment necessary to the servicing of the new Dr. James Ewing Hospital for Cancer to be erected at the center by the city of New York. The new institute will bear the name of the two men who have cooperated in many scientific endeavors, Alfred P. Sloan Jr. and Charles F. Kettering, chairman and vice president and director of research, respectively, of General Motors. Mr. Sloan created the Alfred P. Sloan Foundation to advance in any proper way the interest of the community at large, with emphasis on economic education, giving to it in 1937 an endowment of $10,000,000 to provide for expanded activities.

Deaths in Other Countries

Dr. Henry R. Kenwood, emeritus professor of hygiene and public health, University of London, died June 7, aged 82. ——**Dr. Edward Barclay-Smith,** emeritus professor of anatomy, University of London, died in London, aged 84.——**Dr. Philippe Dally,** noted physician and Paris correspondent of THE JOURNAL, died in Paris July 5, aged 75.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 28, 1945.

The New Chair of Human and Comparative Anatomy at the Royal College of Surgeons

Thanks to the munificence of Sir William H. Collins, a new chair of human and comparative anatomy has been founded at the Royal College of Surgeons. The first to hold it is the distinguished anatomist F. Wood Jones, who occupies the chair of anatomy at the University of Manchester. After graduating in the University of London in 1904 he became demonstrator of anatomy at the London Hospital and St. Thomas's Hospital. After some years as medical officer in the Far East he was appointed anthropologist to the Egyptian government and took part in the archeological survey of Nubia. In 1919 he was appointed professor of anatomy at Adelaide University, which position he resigned in 1927 on taking the Rockefeller chair of physical anthropology in the University of Hawaii. In 1930 he left Hawaii to become professor of anatomy in Melbourne University. In 1932-1933 he acted as director of anatomy in Peiping Union Medical College. He is the author of several books marked by original thinking on corals, arboreal man, the mammals of South Australia, and sea birds as well as "The Principles of Anatomy as Seen in the Hand," "Unscientific Excursions," "Life and Living" and "Design and Purpose."

Inter-Allied Cooperation at the Royal Society of Medicine

This war has to its credit one important benefit—increased contacts between the leaders of the allied countries. In Britain we have been privileged to welcome them in large numbers—from the United States as members of the huge American army quartered here and from the European continent as refugees from German oppression. For the time being they have been honorary members of our medical societies, and the pleasant and profitable contacts with them will be long cherished in our memories. The Royal Society of Medicine, with its membership of over 7,000, has played the leading part in these contacts, of which farewell celebrations have just taken place. At an annual meeting of the fellows the president, Surg. Rear Admiral Gordon-Taylor, presented scrolls of honorary fellowship to certain distinguished persons in medical services of the British and Allied forces. In doing so he addressed the Czech, Norwegian and Belgian recipients in their native languages. The first award was made to Gen. Frantisek Langer, director general of the medical service of the Czech army. The next was made to Dr. Karl Evang, director general of the Norwegian public health services. In returning thanks Dr. Evang said that before the war Norwegian medical science looked to the south, to Germany and Austria, though it had partly turned to Britain and the United States. There would now be a radical change, and more Norwegian doctors would knock at the British door. The last of the allied recipients was Colonel Gallemaerts, director general of medical services of the Belgian army. General Smirnov, head of the medical service of the Russian army, was not able to attend for his presentation. The guests included Brig. Gen. Elliott Cutler of the United States Army in Europe and Col. A. T. Jurasz, dean of the Polish Medical School in Edinburgh. A farewell dinner was also given to the representatives of the Allied forces in this country. The chairman, Sir Henry Tidy, recalled that among the useful subjects discussed by them at the meeting of the society were lifeboats at sea, the psychology of the Germans, army rations, field surgigal units, operational strain, psychosis and combat exhaustion, malaria, head injuries, plastic surgery, the prisoner of war, famine in Bengal, typhus, blood transfusion, infective hepatitis, concentration camps and starvation.

BRAZIL

(From Our Regular Correspondent)

São Paulo, May 26, 1945.

Penicillin in Syphilitic and Parasyphilitic Diseases

Six patients with tertiary yaws were treated with penicillin in small doses at the Evandro Chagas Hospital of the Oswaldo Cruz Instituto in Rio de Janeiro by Dr. F. Nery Guimarães. The lesions presented by the patients were gummatous ulcerations, periostitis, osteitis, osteoporosis and gangoza (rhinopharyngitis mutilans). In all cases clinical recovery was obtained, the time of treatment varying from two to seven months. The number of Oxford units per patient varied from 48,000 to 558,800. Patients with bone lesions, even after treatment, did not show complete repair of the bone structure, but the lesions appeared to be healed and negative serologic tests were obtained.

Dr. Nery Guimarães and his co-workers Drs. Area Leão and Genard Nobrega published their therapeutic researches on syphilitic infection.

Six syphilitic patients were treated with penicillin in small doses at the Evandro Chagas Hospital of the Oswaldo Cruz Institute. Primary lesions were found to be bacterioscopically negative in three to six days, and cicatrized completely in ten to thirteen days with applications of 1,200 to 2,400 Oxford units each in twenty-four hours. Syphilitic condylomas and hypertrophic mucous patches showed negative bacterioscopic results in ten to twenty days with applications of 1,200 Oxford units in twenty-four hours. Doses of 4,800 units during the same time, however, were insufficient to control other secondary syphilitic manifestations (roseolar rash). In 3 cases under serologic control it was found that after a clinical cure had been effected the Wassermann reaction showed considerable oscillation, becoming first negative and then positive.

Brief Items

A postgraduate course in psychiatry and mental hygiene has been inaugurated this month at the Institute of Psychiatry of the University of Rio de Janeiro, under the direction of Prof. Henrique Roxo. Besides Dr. Roxo, Drs. Flavio de Souza, Morais Coutinho, Rodrigo Ulysses and Paulo Lacaz are in charge of the course.

The faculty of the Medical School of the University of Rio de Janeiro conferred the degree of doctor honoris causa on Dr. Pasteur Valéry-Radot, head of the French Cultural Mission to South America, now at Rio de Janeiro.

Marriages

Garrett Michael Swain, Chevy Chase, Md., to Dr. Shirley Catherine Towey of Roselle Park, N. J., in Washington, D. C., May 31.

Thomas A. Keenan, Rutland, Vt., to Miss Christine Elizabeth Kelley of Dorset in New York, April 14.

Norman Blaine Hasler, Worthington, Ind., to Miss Catherine M. McDonald of Orange, Mass., June 14.

William Hugh Hamilton Jr., Hemingway, S. C., to Miss Nanette Sherard of Abbeville, June 23.

Henry Patrick Drake Jr., Marion, Ohio, to Miss Anna Mae Blake of Toledo, June 30.

Arthur Clayton Curtis, Little Rock, Ark., to Miss Grace Roberts of Pine Bluff, June 17.

Robert R. Hays, Akron, Ohio, to Miss Thelma Louise Eppley of Zanesville, May 12.

Jerry Byron Hogsette, Vienna, Ga., to Miss Linda Davis of Sylvania, June 20.

H. W. Davis to Miss Ruth Keene, both of Alton, Ill., June 16.

David Kleiner to Miss Rita Steig, both of Brooklyn, June 30.

Deaths

Egil Thorbjorn Olsen, Detroit; George Washington University School of Medicine, Washington, D. C., 1904; for three years with the U. S. Public Health Service; served as chairman of the program committee of the Wayne County Medical Society, as chairman of the legislative committee of the American Hospital Association and as president of the Michigan Hospital Association; superintendent of the Receiving Hospital from 1929 to 1934; later appointed medical director and assistant superintendent of the Oklahoma University Hospital, Oklahoma City; for many years superintendent of the Englewood Hospital, Chicago; at one time chief medical examiner of the Chicago Civil Service Commission and chief of the bureau of hospitals of the Chicago Health Department; awarded the citation of the Order of Honor and Merit of the Red Cross of Cuba in recognition of services performed in behalf of Cuban residents of Detroit; associated with the medical department of the Ford Motor Company; died in the Henry Ford Hospital June 3, aged 70, of arteriosclerotic heart disease.

James Paul Johnston ✠ East Moline, Ill.; University of Illinois College of Medicine, Chicago, 1922; formerly health officer of East Moline; a member of the Student Army Training Corps at Iowa University during World War I; commissioned a first lieutenant in the Officers Reserve Corps in 1924; began active duty as a first lieutenant in the medical corps, Army of the United States, on Aug. 14, 1942; served at Camp Breckenridge, Ky., the Army Medical Center in Washington, D. C., and the Billings General Hospital in Indianapolis; relieved from active duty as a captain on Nov. 10, 1943; member of the Iowa and Illinois Central District Medical Association and the Association of American Physicians and Surgeons; on the staffs of the Moline Public Hospital, Moline, and St. Anthony's Hospital in Rock Island; taught obstetrics for four years at the Lutheran Hospital in Moline, serving as the 1945 staff president; died in the Veterans Administration Facility, Hines, Ill., June 10, aged 51, of cerebral thrombosis.

Lewis Henry Koplik ✠ New York; Western Reserve University School of Medicine, Cleveland, 1928; diplomate of the National Board of Medical Examiners; member of the New York Academy of Medicine, the Harvard Club of New York, the New York Pathological Society, the American Association of Pathologists and Bacteriologists and the Biological Photographic Association and the New York Pediatric Club; instructor in pediatrics at Cornell University Medical College; assistant health officer at the Kips Bay Yorkville Health Center in New York; interned at the Children's Hospital in Boston and was an instructor in pathology at Harvard Medical School; at the time of his death attending physician and member of the board of the Willard Parker Hospital, where he had been an intern, resident and later visiting physician; died at his summer home at Miller Place, L. I., July 22, aged 41, following an operation for the removal of a pituitary tumor.

Harold Denman Meeker ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1902; formerly professor of surgery at the New York Polyclinic Medical School and Hospital; fellow of the American College of Surgeons; consulting surgeon, New York Polyclinic Hospital; member of the medical board of the Doctors Hospital and a consultant to the Somerset Hospital, Somerville, N. J., Yonkers General Hospital, Yonkers, Broad Street, St. Clare's and Downtown hospitals; in 1927 appointed surgical director to the Reconstruction Hospital and in 1935 honorary surgeon in the police department; awarded an honorary degree of master of science from Wesleyan University; died May 26, aged 69, of cerebral hemorrhage.

Benjamin A. Shepard ✠ Kalamazoo, Mich.; Detroit College of Medicine, 1904; past president of the Michigan Trudeau Society and the Michigan State Tuberculosis Society; past president and secretary of the Kalamazoo Academy of Medicine; past and honorary president of the Kalamazoo Tuberculosis Association; member of the board of directors of the National Tuberculosis Association; fellow of the American College of Physicians and the American College of Chest Physicians; served as medical director of the Pine Crest Sanatorium, Oshtemo; died June 16, aged 65, of coronary occlusion.

Sylvanus F. Basinger, Elyria, Ohio; Cleveland Homeopathic Medical College, 1906; member of the American Medical Association; acting city health commissioner; on the staff of the Elyria Hospital, where he died June 9, aged 67, of chronic myocarditis and pulmonary edema.

Joseph F. Battaglia ✠ Buffalo; University of Buffalo School of Medicine, 1920; school physician for the city health department; on the staffs of Buffalo Hospital of the Sisters of Charity and the Louise de Marillac Maternity Hospital; died June 3, aged 49, of coronary occlusion.

Abraham Louis Blecker ✠ Memphis, Tenn.; Memphis Hospital Medical College, 1912; on the staffs of the Methodist and Baptist hospitals; associated with and in 1929 president of the staff of St. Joseph's Hospital, where he died June 13, aged 58, of uremia.

Fred George Bushold, Lawrence, Mass.; Tufts College Medical School, Boston, 1904; died in the Bessie Burke Memorial Hospital June 8, aged 64, of cerebral hemorrhage.

Charles Willard Cole, Norton, Kan.; Central Medical College of St. Joseph, Mo., 1903; member of the American Medical Association; died May 20, aged 67, of coronary occlusion.

Walter Frank Coleman, Hickory Flat, Miss.; University of Tennessee College of Medicine, Memphis, 1915; member of the American Medical Association; also a druggist; served on the board of aldermen; died June 11, aged 60, of carcinoma.

Rufus George Collins ✠ Chicago; Chicago Medical College, 1885; once on the staffs of the Mercy Hospital and the Michael Reese Hospital, where he died June 24, aged 86, of bronchopneumonia.

George Herbert Davis, East Rochester, N. Y.; University of Vermont College of Medicine, Burlington, 1884; died in the Genesee Hospital, Rochester, April 16, aged 82, of heart disease.

Terence Thomas Dawson, Seattle; Creighton University School of Medicine, Omaha, 1928; member of the American Medical Association; interned at Creighton Memorial St. Joseph's Hospital in Omaha; died May 1, aged 42, of cerebral hemorrhage.

Louis Alfred Dessen ✠ Hazleton, Pa.; Medico-Chirurgical College of Philadelphia, 1911; specialist certified by the American Board of Radiology, Inc.; member of the Radiological Society of North America, Inc., and the American College of Radiology; veteran of the Spanish-American War; consultant radiologist, Hazleton State Hospital; died July 10, aged 65, following an operation for carcinoma of the colon.

John Lydall Dixon, Woodbury, Ga.; Atlanta Medical College, 1895; member of the American Medical Association; died in North East, Pa., May 20, aged 69, of pneumonia.

Warren M. Dodge, Farmington, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1893; died in the Miller Hospital, St. Paul, April 28, aged 78, of carcinoma of the sigmoid.

Edward Sylvester Donnelly, Woodburn, Ore.; John A. Creighton Medical College, Omaha, 1912; died in St. Vincent's Hospital, Portland, May 25, aged 60, of heart disease.

Herschell V. Donovan, Cerro Gordo, Ill.; St. Louis College of Physicians and Surgeons, 1895; died in Chicago June 2, aged 72, of arteriosclerotic heart disease.

Arthur Wheeler Drew ✠ Lieutenant Colonel, U. S. Army, retired, Encinitas, Calif.; Northwestern University Medical School, Chicago, 1913; Medical Field Service School in 1921 and the Army Medical School in 1922; served during World War I; entered the medical corps of the U. S. Army as a first lieutenant on July 1, 1920; retired with the rank of lieutenant colonel on Aug. 31, 1938, for disability in line of duty; died in the U. S. Naval Hospital, San Diego, July 23, 1944, aged 64, of coronary heart disease.

Homan Valentine Duggan ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1893; on the staffs of the Williamsburgh and Wyckoff Heights hospitals; died April 29, aged 73, of coronary disease.

William Lewis Faul, Russellville, Ohio; Cincinnati College of Medicine and Surgery, 1900; member of the American Medical Association; served as county auditor and as county health commissioner; died May 30, aged 70, of carcinoma.

John Grant Foley, Pineville, Ky.; Hospital College of Medicine, Louisville, 1890; member of the American Medical Association; also a dentist; on the staff of the Pineville Community Hospital; died June 12, aged 81, of heart disease.

Robert Sabin Forbes ✠ Duluth, Minn.; University of Pennsylvania School of Medicine, Philadelphia, 1910; fellow of the American College of Surgeons; served during World War I; on the staffs of the Miller, St. Luke's and St. Mary's hospitals; died April 9, aged 58, of cirrhosis of the liver.

Chester Erwin Fulton, Springfield, Mo.; State University of Iowa College of Medicine, Iowa City, 1888; member of the American Medical Association; instrumental in organizing and

erecting the old Springfield Hospital, where he served as surgeon; died May 22, aged 84, of heart disease and uremia.

Jesse Funderburg, Piqua, Ohio; Columbus Medical College, 1886; formerly county coroner; served on the staff of the Piqua Memorial Hospital; died April 14, aged 82, of cerebral hemorrhage.

Robert Wilson Getty, Deer Lodge, Mont.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; member of the American Medical Association; resident on the staff of the Montana State Tuberculosis Sanitarium; served as coroner and deputy health officer of Valley County; died on the train at Gold Creek April 8, aged 77, of coronary heart disease.

Vincent John Grauten ✠ Pittsburgh; University of Pennsylvania School of Medicine, Philadelphia, 1917; served during World War I; on the staff of the Presbyterian Hospital, where he died June 7, aged 55, of carcinoma of the prostate.

Richard Alexander Hale, Houston, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1919; member of the American Medical Association; part owner of the Park View Hospital, where he died May 20, aged 52, of coronary thrombosis.

John Goold Harvey, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; served during World War I; fellow of the American College of Physicians; died in the Veterans Administration Facility, Dearborn, May 24, aged 69, of Buerger's disease and cerebral hemorrhage.

Friedrich Alexander Hecker ✠ Ottumwa, Iowa; University of Kansas School of Medicine, Kansas City, 1913; also a dentist; specialist certified by the American Board of Internal Medicine; member of the Society of American Bacteriologists and the American Society of Clinical Pathologists; fellow of the American College of Physicians; pathologist, St. Joseph Hospital, where he died suddenly June 3, aged 66, of coronary thrombosis.

John Blakeslee Henry ✠ Lawrence, Kan.; University Medical College of Kansas City, Mo., 1903; on the staff of the Lawrence Memorial Hospital, where he died May 8, aged 67, of cerebral hemorrhage.

Thomas James Henry, Apollo, Pa.; Medical Department of the University of Wooster, Cleveland, 1884; member of the American Medical Association; served as vice president of the First National Bank of Apollo; died May 30, aged 86, of cerebral hemorrhage.

Freeman St. Clair Hitchcock ✠ Greenwich, Conn.; New York Homeopathic Medical College, New York, 1907; associated with the Crest View Sanitarium; served on the board of the Neurological Institute in New York; died in the Greenwich Hospital June 7, aged 62, of heart disease.

William Frank Hunt, Davenport, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1896; died in the Mercy Hospital May 26, aged 74, of prolonged fever and influenza.

Milton T. Jay, Portland, Ind.; Medical College of Ohio, Cincinnati, 1890; past president of the Jay County Medical Society; formerly county health commissioner; president of the Jay County Draft Board from 1917 to 1919; a captain in the 139th Field Artillery of the Indiana National State Guard; formerly postmaster; served as president of the board of directors of the Portland City Library; died in Indianapolis May 25, aged 77, of cardiovascular disease.

Markus Frederick Christian Bang Jelstrup, Big Lake, Minn.; Northwestern University Medical School, Chicago, 1903; on the staffs of the Deaconess Hospital, Grand Forks, N. D., and St. Luke's Hospital, Fargo, N. D., died April 10, aged 76, of coronary occlusion followed by angina pectoris.

Michael William Kapp, San Jose, Calif.; Cleveland Medical College, Homeopathic, 1895; member of the American Medical Association; retired member of the California Medical Association; formerly on the staff of San Jose Hospital; died May 28, aged 79, of paralysis agitans.

Thomas S. Kennedy, Eustis, Fla.; Hospital College of Medicine, Louisville, Ky., 1901; Spanish-American War veteran; served as sanitary officer of the West Florida district and assistant state director of rural sanitation; died May 25, aged 67, of massive gastric hemorrhage.

John Kimmel Kiser, Kittanning, Pa.; Cleveland Homeopathic Medical College, 1901; member of the American Medical Association; on the staff of the Armstrong County Hospital; died May 24, aged 69, of hemorrhages from ulcers.

Morris Henry Koch, Allentown, Pa.; Bellevue Hospital Medical College, New York, 1880; member of the American Medical Association; on the staffs of the Sacred Heart Hospital and the Allentown Hospital, where he died in May, aged 86, of senility.

Henry Alfred Lange, Providence, R. I.; College of Physicians and Surgeons, Baltimore, 1909; served in France for the American Red Cross during World War I; on the staff of the Homeopathic Hospital; died in the Rhode Island Hospital May 22, aged 60, of injuries received from a fall, polioencephalitis and hypertensive cardiovascular disease.

Herbert Wood Matthews, Penn Yan, N. Y.; Starling Medical College, Columbus, 1896; member of the American Medical Association; served during World War I; past president of the Yates County Medical Society; formerly chief of staff of the Soldiers and Sailors Memorial Hospital; died June 5, aged 72, of diabetes mellitus.

Frank Alexander May, Palmyra, Ind.; University of Louisville (Ky.) Medical Department, 1909; member of the American Medical Association; on the staff of St. Edward Hospital, New Albany, where he died May 2, aged 62, of postoperative mesenteric thrombosis and gangrene of the gallbladder.

Charles Walsh McQuillen ✠ Charles City, Iowa; State University of Iowa College of Medicine, Iowa City, 1913; on the staff of the Cedar Valley Hospital; died May 30, aged 58, of heart disease.

John Tipton McVey, Bremen, Ohio; Ohio State University College of Medicine, Columbus, 1913; member of the American Medical Association; formerly vice president of the Fairfield County Medical Society; served on the staffs of the Ohio Hospital for Epileptics, Gallipolis, Massillon State Hospital in Massillon and the Columbus State Hospital in Columbus; on the staff of the Lancaster Municipal Hospital, Lancaster, where he died June 7, aged 61, of coronary occlusion.

Nathaniel Kingsbury Noyes ✠ Plymouth, Mass.; Dartmouth Medical School, Hanover, N. H., 1890; a captain in the medical corps of the U. S. Army during World War I; health board physician in Duxbury from 1895 to 1925; visiting physician at the Jordan Hospital for many years; associate medical examiner of the Third Plymouth District for three terms; member of the Massachusetts Association of Health Boards and the Massachusetts Medico-Legal Society; died April 12, aged 80, of heart disease.

Arthur L. Payne, Eau Claire, Wis.; Medical College of Ohio, Cincinnati, 1890; died May 15, aged 79, of coronary thrombosis and diabetes mellitus.

Edward Rayburn Ridley ✠ Detroit; University of Colorado School of Medicine, Denver, 1911; associate physician for the Detroit Edison Company; on the staff of the Harper Hospital, where he died May 30, aged 56, of heart disease and hypertension.

Harry Sloan Saks ✠ Denver; University of Kansas School of Medicine, Kansas City, Kan., 1930; captain, medical reserve corps, U. S. Army, not on active duty; on the staffs of the Beth Israel, St. Anthony and Colorado General hospitals; died May 31, aged 39, of heart disease.

Frank Waldo Scott, Muskogee, Okla.; University of Nebraska College of Medicine, Omaha, 1910; served during World War I; served on the staffs of various Veterans Administration facilities and at the time of his death as chief of the outpatient and reception service, Veterans Administration Facility in Muskogee, where he died April 15, aged 57, of myocardial failure.

Arthur Edgar Smith, Cohoes, N. Y.; University of Vermont College of Medicine, Burlington, 1891; served in the medical corps of the U. S. Army with the rank of captain during World War I; died May 14, aged 81, of acute dilatation of the heart.

William D. Spearman, Social Circle, Ga.; University of Georgia Medical Department, Augusta, 1900; died April 30, aged 69, of angina pectoris.

Frank Spencer, Detroit; Michigan College of Medicine and Surgery, Detroit, 1900; member of the American Medical Association; died in St. Mary's Hospital May 19, aged 73, of bronchopneumonia.

Martin Frank Wright, Burlington, W. Va.; University of Maryland School of Medicine, Baltimore, 1890; member of the American Medical Association; served as president and secretary-treasurer of the Potomac Valley Medical Society and as vice president of the state medical association; in 1943 made honorary life member of the West Virginia State Medical Association; died June 21, aged 75, of cerebral hemorrhage.

MARTYRS IN THE SINKING OF THE U. S. S. COMFORT

The Hospital Ship was attacked April 28 by a Japanese "suicide" pilot off the coast of Okinawa

CAPT. CHARLES D. CLARK, M. C., A. U. S., 1909-1945

CAPT. WILLIAM A. MACPHERSON, M. C., A. U. S., 1907-1945

MAJOR EDWIN BRECK ECKERSON, M. C., A. U. S., 1905-1945

Charles Dougherty Clark, South Bend, Ind.; Wayne University College of Medicine, Detroit, 1939; interned at the Grace Hospital in Detroit and served a residency at the Royal Oak Hospital in Royal Oak, Mich.; medical director of the Bendix-Aviation Corporation; began active duty as a captain in the medical corps, Army of the United States, on July 1, 1942; aged 35.

William Alexander Macpherson ✠ Downey, Calif.; College of Medical Evangelists, Los Angeles, 1935; interned at the Orange County Hospital in Orange; diplomate of the National Board of Medical Examiners; specialist certified by the American Board of Ophthalmology; served as assistant physician on the staff of the Sage Memorial Hospital in Ganada, Ariz., and on the staffs of the Los Angeles County Hospital in Huntington Park, the Bell Mission Hospital in Bell and the Suburban Hospital in South Gate; began active duty as a captain in the medical corps, Army of the United States, on Oct. 15, 1942; assigned to BTC number 5, Army Air Forces Technical Training Command in Kearns, Utah; aged 38.

Edwin Breck Eckerson ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1931; diplomate of the National Board of Medical Examiners; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons and the New York Academy of Medicine; member, New York Surgical Society; instructor in surgery at his alma mater; member of the board of directors and assistant attending surgeon at St. Luke's Hospital, where he served an internship; assistant attending surgeon at the New York Post-Graduate Medical School and Hospital and the Mount Vernon (N. Y.) Hospital; formerly resident at Lahey Clinic, Boston; began active duty as a captain in the medical corps, Army of the United States, on May 14, 1942; later promoted to major; chief surgeon on the U. S. S. *Comfort;* aged 39.

Ernest Foss Jr., Newburyport, Mass.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1941; interned at the Rochester General Hospital in Rochester, N. Y.; began active duty as a first lieutenant in the medical corps, Army of the United States, on July 15, 1942 and assigned to the 19th General Hospital at Camp Livingston, La.; later promoted to captain; aged 31.

Wallace Lea Chesbro ✠ Lieutenant Commander (MC), U. S. Navy, Springfield, Mass.; Tufts College Medical School, Boston, 1938; interned at the Boston City Hospital; served a residency at the Robert Breck Brigham Hospital in Boston; began active duty as a lieutenant (jg) in the medical corps, U. S. Naval Reserve, on March 17, 1941; entered the medical corps of the regular navy as a passed assistant surgeon in the same rank on April 29, 1942; subsequently promoted to the ranks of lieutenant and lieutenant commander; aged 31.

John Francis O'Brien Jr., Waterford, Conn.; Georgetown University School of Medicine, Washington, D. C., 1943; interned at St. Francis Hospital in Hartford; began active duty as a first lieutenant in the medical corps, Army of the United States, on Oct. 6, 1944; trained at Carlisle Barracks, Pa., and at Moore General Hospital, Swannanoa, N. C.; aged 27.

CAPT. ERNEST FOSS JR., M. C., A. U. S., 1914-1945

LIEUT. COMDR. WALLACE L. CHESBRO (MC), U.S.N., 1913-1945

LIEUT. JOHN FRANCIS O'BRIEN JR., M. C., A. U. S., 1917-1945

Correspondence

A MEXICAN TREATMENT FOR CANCER—A WARNING

To the Editor:—Many cancer patients from the United States have recently been attracted to Mexico City by reports of a new, allegedly successful method of treatment. We have taken occasion carefully to investigate the situation and we have prepared this statement of our opinion for the benefit of our colleagues who may be wondering about the matter.

Personal investigations reveal a modernistic building for hospitalization with inadequate laboratory or other scientific facilities. The physician in charge has a courteous and considerate bedside manner. We think that he makes his patients feel better by virtue of his personality. There is no positive evidence that he or his associates are successful by their peculiar methods in interrupting the usual course of a malignant process.

The theoretical bases for the method of treatment are extraordinary. While they make use of current scientific concepts, they are not in accord in any way with established biochemical or pathologic considerations. It is proposed that local sensitivity to pain is determined by the acid-base reaction of tissues. It is claimed that general sensitivity to pain can be estimated from urinary reaction. Alterations may then be made in diet or by medication, to change urinary p_H, in order to relieve sensitivity to pain. There is no objective satisfactory scientific evidence to support these ideas. In a similar way, a theory has been elaborated to cover various aspects of the control of malignant growth. Practically this results in the preparation of various glandular and tissue brews which are digested in various ways for parenteral and oral administration. No positive evidence exists to indicate the value of these preparations in treating malignancy.

A characteristic but unfortunate aspect of the matter is that no satisfactory clinical records are kept. Various statements are made from time to time in notebooks, but no attempt has been made, as far as we know, to provide clinical records that would be at all acceptable for clinical appraisal according to modern standards.

It is concluded that little benefit may result from cancer patients going to Mexico City for this new "treatment."

Chauncey D. Leake, Ph.D., Galveston, Texas.
E. W. Bertner, M.D., Houston, Texas.
C. A. Calhoun, M.D., Houston, Texas.
R. T. Cooksey, M.D., Madison, Wis.
Lowell S. Goin, Los Angeles.
Wellwood Nesbit, M.D., Madison, Wis.
Charles Phillips, M.D., Temple, Texas.
Harold P. Rusch, M.D., Madison, Wis.
William D. Stovall, M.D., Madison, Wis.

FIRST AID FOR IVY POISONING

To the Editor:—As one who is allergic to ivy poison, I was of course interested in the editorial in The Journal, June 23. Some thirty years ago I suffered from a violent dermatitis, which came on promptly after beginning to use my fur gloves that had been moth proofed with synthetic camphor. The discomfort was intense and resistant to everything I tried. The eruption was similar to that of an intense ivy poisoning. In desperation, after the condition had run on for about a week, I thrust my wrists under the stream from the hot water faucet, in and out quickly to avoid scalding. At first the itching was so much intensified that it was almost a pleasure, but each succeeding plunge brought less response, until the itching was entirely relieved after about a dozen applications and remained so for several hours. I repeated the same course of treatment, and the whole thing cleared up in a day or two. Following this clue, I tried the scalding hot water treatment in other cases of pruritus, including several of ivy poison, with the same result. A beginning case of ivy poison can be immediately stopped from itching and will dry and frequently will not even need a second treatment. I was infected several times this spring myself, as we have a lot of the stuff growing about my home. One treatment suffices to cure it and I do not give it a second thought. This has been my only treatment for this condition and it always works. I have used it with the same success in practically all the different forms of pruritus that have come under my care.

Francis E. Park, M.D., Boston.

DEVELOPMENT OF RED BLOOD CELLS

To the Editor:—I was interested in the answer to a question in The Journal, June 16, page 552, regarding the development of red blood cells, since it cites my 1938 article as the sole reference. There are, however, certain corrections and additions which are necessary in order to make your reply not only more accurate but also more practical and functional.

The idea set forth in the first sentence of your answer is essentially the one which some of us have been trying to put across for a number of years. However, the influence of Doan, Cunningham and Sabin has been so great during the past twenty years that it will be a long time before many of our largest and best medical schools realize the correctness of your first sentence. From personal experience in the East during the last eight years I would say that the majority of investigators do not believe that there are two generations of red blood cells.

The terminology which you suggest has been used by some of our histologists (Bloom) for a number of years and represents one of the schemes adopted by Maximow. However, clinical pathologists and general pathologists, especially in Europe, have been favoring the use of the term erythroblast alone in the general sense and not for a specific stage of red cell development. Not a few, but a vast majority, of authorities outside the United States use the term normoblast for all precursors of the definitive series. In our country there is a definite trend in that direction among the Midwestern clinicians, but not so with histologists. Such a classification has its merits when applied to a study of red blood cell development in pernicious anemia before and after treatment, where we recognize a megaloblastic series in the former and a normoblastic series in the latter.

The problem of red cell development is not solved, nor is it likely to be in the near future. Perhaps it is for the histologist but not so for the pathologist. For example, instances have been reported in which the patient, sometimes a child, appears to have a temporary or partial deficiency of anti-pernicious anemia principle. The red blood cell development does not seem to be either normoblastic or megaloblastic. Lambin and de Weerdt have described intermediate erythroblasts. I have been reluctant to recognize such a cell line until recently.

Any exposition of the red cell problem which cites my work as a reference would certainly be incomplete and inaccurate without some mention of the importance of nuclear structure as a means of cell identification. Bloom and his school have maintained that the greatest difference in appearance between the primitive and definitive generations is one of size. However, when dry smears are made of blood from the yolk sac, umbilical cord, fetal liver and bone marrow it is found that, regardless of cell size, the nuclear pattern is quite characteristic and distinctive. More and more emphasis should be placed on the value of nuclear structure in order for clinicians and pathologists to interpret properly blood and bone marrow cells.

Oliver P. Jones, Ph.D., Buffalo.
Professor and Head of Anatomy, University of Buffalo School of Medicine.

MORE ON MARIHUANA AND MAYOR LA GUARDIA'S COMMITTEE REPORT

To the Editor:—I read Dr. Bowman's communication, which appeared in THE JOURNAL, July 21.

There has come to my desk a reprint of an article from the *Indian Journal of Medical Research*, January 1942, entitled "Cannabis Sativa in Relation to Mental Diseases and Crime in India," by Col. Sir R. N. Chopra, who has been conducting a drug addiction inquiry for many years at the School of Tropical Medicine, Calcutta, India. Dr. Chopra is the author of "Tropical Therapeutics." The investigations by Dr. Chopra and his associates cover many years of scientific study, and their findings are representative of the entire population.

Some of Dr. Chopra's studies on hemp drug addiction in India were published in July 1939 in the *Indian Medical Research Memoirs*. His recent report on "Cannabis Sativa in Relation to Mental Diseases and Crime in India" is the result of long intensive study of 1,800 hemp drug addicts and destroys most of the conclusions of the New York Mayor's Committee, which studied, according to Bowman, 72 prisoners and 5 volunteers for a comparatively short period. The Chopra report indicates profound knowledge and prolonged study of the problem. Six hundred established cases of hemp drug insanity were studied and 1,238 hemp drug addicts were studied to show the relation between addiction to hemp drugs and crime.

The report summarizes that "excessive indulgence in narcotics, such as Indian hemp, is apt to produce in healthy individuals and in susceptible individuals mental confusion which may lead to delusions with disorientation and disordered movements. . . . Sometimes it may release subconscious impulses and lead to violent crime. . . . Inquiries in various jails and mental centers revealed that in quite a number of cases simple indulgence even in a single ganja or charas (marihuana) smoke was responsible for a heinous crime. . . . Fits of aggressive mania are not infrequently observed after indulgence in hemp drugs. Impulses of a suicidal and morbid nature have been known to occur. . . . Our studies in mental hospitals in the field (tables I and VII) and in prisons show that not infrequently addiction to hemp drugs was the immediate cause of a sudden unbalance of mind and the commission of a crime."

A copy of this article will be mailed free of charge to any one addressing a request to the U. S. Bureau of Narcotics, Tower Building, 14th and K streets N.W., Washington, D. C.

H. J. ANSLINGER, LL.B., Washington, D. C.
U. S. Commissioner of Narcotics.

WHOLE BLOOD AND CITRATED BLOOD

To the Editor:—Dr. Scannell's communication in THE JOURNAL, June 23, attempts to correct what he considers to be an error and brings to light a skeleton which most of us thought had been securely and permanently locked away in a closet.

The term "whole blood" has been most frequently applied to blood obtained from so-called live donors and administered by the direct method of transfusion. Others have applied the term to citrated or preserved blood. As has been pointed out repeatedly, both views are incorrect. Strictly speaking, whole blood must be a substance from which none of its component parts have been removed—cells, serum and/or plasma. Any of these components may be used separately according to indication, and they make up what might be referred to as whole blood but should simply be designated as "blood." When blood is mixed with an anticoagulant or preservative it might be called, as has been suggested, "modified blood."

The statement "Whole blood and citrated blood are as different as black and white" is therefore entirely erroneous. It serves only to create further confusion.

I must also take exception to the statement "severe reactions following the use of citrated blood are far more frequent than when whole blood is used." It is safe to state that most workers are now agreed that such is not the case. Certainly the literature affords ample proof to the contrary, and statistics of blood banks furnish further proof (Geiger, Jacob: History of Blood Transfusion, *Exper. Med. & Surg.* **2**:83 [Feb.] 1944). May I quote from the annual report of the Lincoln Hospital Blood Bank for the year 1944:

Total number of transfusions	1,348
Modified blood (citrated bank blood)	1,018
Indirect blood transfusions (bank blood)	1,017
Direct blood transfusion ("live donor")	1
Pooled plasma (prepared from bank blood)	278
Resuspended cells	52
Reactions:	
1. Severe (hemoglobinuria in a case of hemolytic anemia)	1
2. Minor	
(*a*) Urticaria	12
(*b*) Pyrogenic	5
Percentage of severe reactions	0.07
Percentage of minor reactions	1.3

Finally I should like to point out that in Lincoln Hospital we instituted the practice of routine Rh determination in the latter part of the year. While the Rh factor may unquestionably be responsible for an occasional severe reaction, and while we heartily endorse this precautionary step, we cannot agree with the conclusion that, "as a result reactions have been eliminated when whole blood is used." Transfusion reactions can and must be kept at a minimum, but they must still be classified as (1) avoidable and (2) unavoidable. Let us concentrate on the avoidable reactions and not quibble about those that are unavoidable.

JACOB GEIGER, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Aug. 11, page 1125.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various centers, Jan. 18. *Oral.* Various centers, Oct. Final date for filing application is Oct. 20. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York 24.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May 27. Final date for filing application is Feb. 1. Sec., Dr. P. C. Bucy, 912 S. Wood St., Chicago 12.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 2. Final date for filing application is Nov. 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: Chicago, Oct. 2-5 and Los Angeles, Jan. 18-22. Sec., Dr. S. Judd Beach, 56 Ivie Rd., Cape Cottage, Me.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 3-6. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City, Ia.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Oct. 19. *Oral.* New York, Dec. 7-8. Sec., Dr. C. A. Aldrich, 115½ First Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: *Written.* Various centers, Dec. 9. *Oral.* Chicago, February 1946. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis 4.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1935 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

29:555-660 (May) 1945

Chronic Auricular Tachycardia with Unusual Response to Change in Posture: Report of 2 Cases. R. Miller and J. S. Perelman.—p. 555.
Wolff-Parkinson-White Syndrome: Report of 5 Cases. R. W. Robinson and W. G. Talmadge.—p. 569.
*Prognostic Significance of Auricular Fibrillation in Association with Myocardial Infarction. J. M. Askey and O. Neurath.—p. 575.
*Gastrointestinal Symptoms of Progressive Myocardial Disease. R. L. McMillan, F. E. Cowden and J. B. Reinhart.—p. 580.
Coronary Occlusion in Industry: A Study of 84 Cases with Reference to Subsequent Employability. E. B. Levine and E. Phillips.—p. 588.
Relation of Resting Heart Rate to Increase in Rate Due to Exercise. W. W. Tuttle and Elizabeth Powell Salit.—p. 594.
Acute Bacterial Endocarditis in the Aged. F. D. Zeman and S. Siegal. —p. 597.
Auricular Heart Sounds in Auricular Flutter. H. H. Hecht and G. B. Myers.—p. 610.
Acute Benign Pericarditis: Report of 2 Cases in Young Adults. W. G. Talmage.—p. 623.
Electrocardiographic Changes in Active Duodenal and Gallbladder Disease. N. E. Clarke.—p. 628.
Momentary Atrial Electrical Axes: III. A-V Nodal Rhythm. A. Ruskin and G. Decherd.—p. 633.
Orchitis and Hydrocele After Cardiac Infarction. B. Kisch.—p. 641.
Silicosis of Pericardium: Case Report. Marguerite G. Stemmerman. —p. 642.
Congenital Tricuspid Insufficiency: Report of Case. Viola G. Brekke. —p. 647.

Auricular Fibrillation with Myocardial Infarction.—Askey and Neurath studied 84 patients with auricular fibrillation observed among a group of 1,247 patients with myocardial infarction admitted to the Los Angeles County Hospital, an incidence of 7.7 per cent. The diagnosis of myocardial infarction was accepted only when the history and the electrocardiogram were typical. Auricular fibrillation was diagnosed only when confirmed by electrocardiograms. The mortality rate among patients with a myocardial infarction plus auricular fibrillation was much higher than in a group without auricular fibrillation. If the auricular fibrillation disappeared in one day, the mortality rate was slightly increased; if it persisted longer than one day, the mortality rate increased greatly. If no reversion to sinus rhythm occurred, death ensued in 89 per cent. One third of the deaths were due to systemic emboli. Persistence of arrhythmia could be correlated with preexisting cardiac damage. Cardiac damage, however, was not the sole cause of the high mortality rate and high incidence of embolism. Auricular fibrillation increased the mortality rate and incidence of embolism regardless of whether congestive failure was or was not present. Whether or not auricular fibrillation was found in the first electrocardiogram was a fairly reliable way of predicting whether the arrhythmia would be persistent or transient. In only 8 of the 55 cases in which auricular fibrillation was found in the first tracing did the arrhythmia disappear, whereas in 27 of 35 in which the arrhythmia followed myocardial infarction sinus rhythm returned. If the auricular fibrillation followed myocardial infarction, the prognosis was about the average if it disappeared in one day or less, but if it lasted more than one day the prognosis was much worse because then the arrhythmia persisted in about one third. The worst prognosis was among those whose auricular fibrillation was known to have existed before (99 per cent mortality with 57 per cent dying of systemic embolism) and among those who had a previous infarct (96 per cent mortality, with 30 per cent systemic embolism).

Gastrointestinal Symptoms of Heart Disease.—McMillan and his associates state that, when nausea and vomiting are dominant symptoms in a case of heart failure, one should not only consider as possible factors drugs, congestion of the abdominal viscera and disorders of the blood metabolites (such as occur in uremia) but should also entertain the possibility that progressive myocardial disease may be the cause of the symptoms. The mechanism of nausea and vomiting induced by progressive myocardial disease is believed to be analogous to that caused by digitalis, which has been shown to be due to a reflex arising in the heart itself. When coronary thrombosis occurs in a patient with preexisting narrowing of the smaller arterial branches a vicious cycle may ensue; the decline in the cardiac output and small pulse pressure lead to a further coronary insufficiency and progressive myocardial fibrosis, which brings about a further decrease in the cardiac output. In cases of heart failure in which there is a small pulse pressure with a high diastolic pressure, the outlook is poor.

American J. Digestive Diseases, Fort Wayne, Ind.

12:187-218 (June) 1945

Some Biologic Considerations of Gallstones. H. Gauss.—p. 187.
Etiology of Peptic Ulcer: New Hypothesis. R. A. Steven.—p. 192.
Changes in Volumes of Blood and Extracellular Fluid in Bowel Obstruction of Rabbit. C. A. Ender and R. C. Herrin.—p. 193.
Effect of Aluminum Hydroxide on Food Utilization in Human Subjects. R. D. Grondahl and E. S. West.—p. 197.
Some Effects of Magnesium Trisilicate Ingestion on Blood, Urine and Feces of Human Subjects. E. S. West and C. Pennoyer.—p. 199.
Incidence of Gastritis in Gastric Ulcer. J. L. Horner and H. Scheff. —p. 202.
Luetic Rectal Stricture. A. Melamed and S. M. Feld.—p. 203.
Differential Diagnostic Problems in Diseases of Mesenteric Glands. E. Muehsam.—p. 206.

American J. of Obstetrics and Gynecology, St. Louis

49:719-830 (June) 1945

Estimation of Work of Obstetric Labor and Its Significance in Heart Disease. J. J. Sampson, Elise M. Rose and R. Quinn.—p. 719.
Comparative Action of Posterior Pituitary and Ergonovine in Third and Fourth Stages of Labor: Observations Based on 5,000 Deliveries. M. Leff.—p. 734.
Supravesical Extraperitoneal Cesarean Section (Waters' Type): Experience with 250 Operations. E. G. Waters.—p. 739.
*Sulfonamide Therapy in Gonococcal Infection in Women: Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfadiazine. H. C. Hesseltine, Lucile R. Hac, F. L. Adair and D. K. Hibbs.—p. 746.
Exercises in Dysmenorrhea. J. O. Haman.—p. 755.
Therapeutic Interruption of Pregnancy. Katherine Kuder and W. F. Finn.—p. 762.
Pregnancy in Rudimentary Horn of Uterus. F. W. Muslow.—p. 773.
Postoperative Vesicouterine Fistula. R. T. Frank.—p. 776.
Carcinoma Following Pregnancy with Spontaneous Cure. W. Levine and S. Weiner.—p. 778.
Pregnancy After Renal Biopsy in Hypertensive Disease. R. S. Siddall. —p. 782.
Demonstration Model for Uterotubal Insufflation. I. C. Rubin.—p. 786.
Surgical Treatment of Absence of Vagina: Report of 2 Cases. F. E. Whitacre and C. Y. Che.—p. 789.

Sulfonamide Therapy in Gonococcic Infection in Women.—Hesseltine and his associates report a four year study of sulfonamide therapy in gonococcic infection in women. They have treated 1,126 women with sulfanilamide, sulfapyridine, sulfathiazole or sulfadiazine. Criteria of cure required that patients be observed at least two months following therapy before they could be discharged as cured. A follow-up study was made on 575 patients who were discharged as cured or who failed to respond to therapy. Of these, 430 (75 per cent) responded to one course of therapy and were discharged cured; 145 had repeated or recurrent positive cultures and received further therapy. The authors arrive at the following conclusions: Sulfadiazine is the drug of choice for treatment of gonococcic infection of women. Sulfathiazole is slightly less effective. Both drugs gave better results and were better tolerated than sulfanilamide or sulfapyridine. Diagnosis of gonorrhea and criteria of cure, wherever possible, should be based on cultural studies. Patients should be observed through at least one negative menstrual period and preferably two. Negative smears and cultures taken just after the menstrual period should be required. Considerable information is obtained from cultures taken during therapy. The menstrual period is

the best provocative test. Complications of salpingitis or bartholinitis were not associated with more failures of therapy than acute uncomplicated cases. Drug fast strains were produced in the adult women in less than 1 per cent of the cases.

American Journal of Surgery, New York

68:279-406 (June) 1945

Air Embolism, with Special Reference to Its Surgical Importance. H. S. Martland.—p. 281.
Hernia in Infancy and Childhood. A. H. Iason.—p. 287.
Pediatric Urologic Problem Important to General Practitioner. R. U. Whipple.—p. 297.
Primary Omental Torsion. J. I. Anton, J. E. Jennings and M. B. Spiegel.—p. 303.
Intercostal Nerve Block in Balanced Anesthesia. S. Belinkoff.—p. 318.
Operation for Anal Fistulas: Some Reasons for Failures. R. J. Jackman.—p. 323.
Fixity of Facial Expression Following Undermining of Skin Over Nose: Modified Method by Which It Is Avoided. A. P. Seltzer.—p. 326.
Failure of Cure of Pelvic Infections Following Use of Penicillin. T. B. Marwil.—p. 336.
Prosthetic Restorations After Amputations About the Hand. A. M. Brown.—p. 338.
Transverse Incision for Appendectomy. S. D. Murray.—p. 344.
Clinical Use of Red Cell Amino Acid Mixture as Substitute for Whole Blood Transfusions. B. G. P. Shafiroff, I. S. Barcham and H. Doubilet. —p. 348.
Bridge Operation for Dupuytren's Contracture. L. A. Palmer and J. L. Southworth.—p. 351.
Response to Preoperative Irradiations as Clue to Management of Breast Cancer. L. M. Levi.—p. 355.

Annals of Internal Medicine, Lancaster, Pa.

22:639-772 (May) 1945

Heart Disease in Jungles of South Pacific: Some Observations Made Among Melanesians of New Hebrides and Solomons Islands Area. A. S. Hyman.—p. 639.
Comparative Value of Several Liver Function Tests. M. Teitelbaum, A. C. Curtis and S. M. Goldhamer.—p. 653.
Clinical Use of New Types of Modified Protamine Zinc Insulin. R. Sanz del Fierro and E. L. Sevringhaus.—p. 667.
Abdominal Manifestations of Rheumatic Fever: Description of Right Rectus Syndrome. N. Reitman.—p. 671.
Anorexia Nervosa: Diagnosis and Treatment of Inanition Resulting from Functional Disorders. J. M. Berkman.—p. 679.
Electroconvulsive Shock Therapy and Cardiovascular Disease. V. L. Evans.—p. 692.
Present Status of Chemotherapy in Tuberculosis. H. C. Hinshaw, W. H. Feldman and Karl H. Pfuetze.—p. 696.
*Bronchospirometry. M. Pinner, G. C. Leiner and W. A. Zavod.—p. 704.
Duodenal Ulcer, with Perforation Following Cutaneous Burn. V. W. Koch and W. A. Fischer.—p. 719.

Bronchospirometry.—Pinner and his associates present a summary of the results of bronchospirometric studies which were pursued at the Montefiore Hospital, New York. The use of a soft rubber tube, instead of the metal bronchoscope, has made the method less uncomfortable and more reliable. Bronchospirometry is indicated whenever an irreversible operation on one lung is contemplated in order to determine the functional capacity of the contralateral lung. It also permits the study of various physiopathologic problems. Spirometry may give nearly normal findings on patients in whom bronchospirometry reveals extensive damage of one lung and compensatory changes in the other lung. X-ray and clinical findings do not permit definite conclusions as to pulmonary function. Pleural involvement often causes severe functional damage of the lung, whereas parenchymal lesions may have relatively little effect on pulmonary function. During pneumothorax treatment the collapsed lung shows the following changes: decrease of oxygen intake, minute volume, tidal air, vital capacity, reserve air and complementary air; increase of ventilation equivalent. Compensation is achieved by an increase of the oxygen intake in the contralateral lung. This is done only in part by increased ventilation; oxygen intake is further increased by a better utilization of the ventilated oxygen, i. e. a decrease of the ventilation equivalent. The contralateral effect of unilateral pneumothorax is manifested by a decrease of the vital capacity, reserve and complementary air of the contralateral lung. Thoracoplasty causes similar functional changes as does the pneumothorax but, on the average, these changes are less severe following thoracoplasty than those during collapse by pneumothorax and, at least in some cases, less severe than those in lungs following the abandonment of pneumothorax. Lungs reexpanded following pneumothorax treatment frequently show extensive functional impairment. Change in the patient's posture from the recumbent to the left or right side does not affect the percentage distribution of the vital capacity between the left and the right lung. Attempts at immobilizing a hemithorax by sandbags weighing up to 20 pounds and by strapping with adhesive tape do not achieve a reduction of the ventilation or respiratory work of the underlying lung.

Bull. of the U. S. Army Med. Dept., Washington, D. C.

89:1-122 (June) 1945

Infantry Battalion Medical Section in Combat.—p. 80.
New Plastic Orbital Implant. J. R. Nieder and J. L. Campbell Jr. —p. 88.
Cross Connection Hazards in Military Hospitals. S. C. Martin.—p. 90.
*Waldmann Vaccine for Foot and Mouth Disease in Liberated Italy, 1944. R. W. Rushmore.—p. 94.
Trench Foot: Diagnostic Value of "Ischemic Pain." A. E. Schecter and C. A. Ragan.—p. 98.
March Fracture of First Rib (Barrack Bags Fracture). S. E. Proctor, T. A. Campbell and A. S. Abramson.—p. 101.
Intrapericardial Use of Penicillin. L. B. Smith and W. P. McHugh. —p. 106.
Modification of Eve Method of Resuscitation. S. B. Lapin.—p. 110.

Waldmann Vaccine for Foot and Mouth Disease.—Rushmore says that late in 1944 the Veterinary Corps of the Army of the United States produced and distributed 36,000 adult bovine doses of the vaccine. There has not been a reported incidence of the disease in any 1 of the 36,000 vaccinated animals. In Rome Province 15,000 dairy cattle and calves were vaccinated in September and October. During the first week in November a herd of 280 nonvaccinated dairy cattle and calves centrally located in Rome Province became infected, with a mortality of 20 calves and 7 cattle. Four months later none of the 15,000 vaccinated animals have reportedly shown any symptoms of the disease, though the infection was reported in 6 nonvaccinated dairy herds.

Florida Medical Association Journal, Jacksonville

31:499-550 (May) 1945

Gallbladder Disease as Related to Anatomic and Physiologic Abnormalities. E. B. Campbell.—p. 521.
History of Medicine in Duval County: Part IV. W. Merritt.—p. 523.

31:551-606 (June) 1945

Inguinal Hernia in the Army. M. N. Camp.—p. 575.
Wartime Problems of Local Health Department. W. W. Rogers.— —p. 578.

Hawaii Medical Journal, Honolulu

4:231-262 (May-June) 1945

Surgical Lessons Learned in World War II. H. K. Gray.—p. 233.
Advances in Surgery During Present War. F. Raine.—p. 236.
Medical Lessons Learned in World War II. H. L. Meltzer.—p. 239.
Clinical Advances in Medical Problems Occasioned by World War II. A. W. Hobby.—p. 243.
Aims and Aspirations of Territorial Association of Plantation Physicians. H. M. Patterson.—p. 246.

Journal of Experimental Medicine, New York

81:539-666 (June) 1945

Comparison of Effects of Pyridoxine and Pantothenic Acid Deficiencies on Nervous Tissues of Swine. R. H. Follis and M. M. Wintrobe. —p. 539.
Cellular Dynamics in Intestinal Mucosa: Effect of Irradiation on Epithelial Maturation and Migration. N. B. Friedman.—p. 553.
Individual Blood Differences in Mexican Indians, with Special Reference to Rh Blood Types and Hr Factor. A. S. Wiener, J. Preciado Zepeda, Eve B. Sonn and H. R. Polivka.—p. 559.
Proteolytic Enzyme Produced by Group A Streptococci, with Special Reference to Its Effect on Type Specific M. Antigen. S. D. Elliott. —p. 573.
Loss of Group Carbohydrate During Mouse Passages of Group A Hemolytic Streptococcus. A. T. Wilson.—p. 593.
Neoplastic Potentialities of Mouse Embryo Tissues: I. Findings of Skin of C Strain Embryos Transplanted to Animals. P. Rous and W. E. Smith.—p. 597.
Neoplastic Potentialities of Mouse Embryo Tissues: II. Contributory Experiments: Results with Skin of C3H and Webster-Swiss Embryos: General Considerations. W. E. Smith and P. Rous.—p. 621.
Studies on Denaturation of Antibody: II. Effect of Protein Concentration on Rate of Denaturation of Diphtheria Antitoxin by Urea. G. G. Wright.—p. 647.

Journal of Nutrition, Philadelphia

29:365-438 (June) 1945

*Acute and Chronic Ascorbic Acid Deficiencies in Rhesus Monkey. J. H. Shaw, P. H. Phillips and C. A. Elvehjem.—p. 365.
Availability of Vitamins from Yeasts: I. Absorption of Thiamine by Human Subjects from Various Types of Bakers' Yeast. Helen T. Parsons, Anne Williamson and Mary L. Johnson.—p. 373.
Id.: II. Accessibility to Rats for Growth of Thiamine in Various Types of Bakers' Yeast. Helen T. Parsons, Audrey Foeste and Helen Gilberg.—p. 383.
Retention of Thiamine, Riboflavin and Niacin in Cooking Pork and in Processing Bacon. S. H. Jackson, A. Crook, V. Malone and T. G. H. Drake.—p. 391.
Dental Caries in the Cotton Rat: III. Effect of Different Dietary Carbohydrates on Incidence and Extent of Dental Caries. B. S. Schweigert, J. H. Shaw, P. H. Phillips and C. A. Elvehjem.—p. 405.
Relation Between Absorbed Nitrogen, Nitrogen Balance and Biologic Value of Proteins in Adult Dogs. J. B. Allison and J. A. Anderson.—p. 413.
Nutritional Value of Yeast Protein to Rat and Chick. A. A. Klose and H. L. Fevold.—p. 421.
Effect of Feeding Succinylsulfathiazole to Rats Receiving Purified Diets High in Carbohydrate, Protein, Fat or Protein and Fat. L. D. Wright, Helen R. Skeggs and K. L. Sprague.—p. 431.

Ascorbic Acid Deficiencies in Rhesus Monkeys.—Shaw and his associates produced ascorbic acid deficiency in Rhesus monkeys. Acute deficiency could be produced in young monkeys in from thirty to fifty days. In the acute phase there was a precipitous loss of weight, slight tenderness of the joints and heavy residues on the tooth surfaces. No gingival changes were observed. When a single test dose of ascorbic acid was given, there was a rapid and complete alleviation of these signs. In the chronic state of ascorbic acid deficiency a series of gingival changes was observed which was accompanied by increasing food deposits on the teeth and dental tartar. There was severe tenderness and soreness at all the joints accompanied by a considerable swelling. Bone resorption occurred on the bone cartilage junctions, especially at the ends of the long bones of the legs. Late in the chronic deficiency period a severe loss of hair was observed, and there was some dermatitis. After a month of treatment with ascorbic acid there had been a moderate increase in weight, a great increase in activity and a loss of soreness about the joints. There had been no improvement in the hair coat. Both the loss of hair and the dermatitis could be cured or prevented by the administration of crystalline biotin. In 3 of the 6 chronically deficient monkeys there was a high incidence of dental caries. These data indicate that the signs of acute chronic ascorbic acid deficiencies in monkeys are distinctly different. They may partially explain the differences observed in experimentally produced and in spontaneous scurvy in man.

Oklahoma State Medical Assn. Jour., Oklahoma City

38:189-234 (May) 1945

Responsibility of Physician in Preventive Proctology. E. Moore.—p. 189.
Survey of Extraocular Motor Anomalies. C. A. Royer.—p. 191.
Political Control of Medicine. G. H. Garrison.—p. 195.

38:235-276 (June) 1945

Common Eye Conditions Among Military Men. W. W. Sanger.—p. 235.
Tonsillectomy in Young Children with Allergy. G. C. Moore.—p. 238.
Cancer of Rectum and Rectosigmoid. R. L. Murdoch.—p. 239.

Public Health Reports, Washington, D. C.

60:577-604 (May 25) 1945

*Serial Passage of Plasmodium Gallinaceum in Chick Embryos. V. H. Hass, H. A. Feldman and Frances M. Ewing.—p. 577.
Universal Type Concrete Slab for Precast Ditch Linings. W. V. Parker and H. A. Johnson.—p. 582.
*Growth of Pasteurella Tularensis in Yolk Sac of Developing Chick Embryo. C. L. Larson.—p. 587.

60:605-632 (June 1) 1945

Comparative Potencies of Several Typhus Vaccines. R. Donovick and R. W. G. Wyckoff.—p. 605.
Sickness Absenteeism Among Industrial Workers, Fourth Quarter of 1944, with Note on Seasonal Variation. W. M. Gafafer.—p. 612.

Serial Passage of Plasmodium Gallinaceum in Chick Embryos.—Haas and his associates have carried Plasmodium gallinaceum through fourteen serial passages by inoculating 10 to 13 day old chick embryos intravenously with parasitized blood. The infection produced in chick embryos by this method is highly fatal, with the majority of deaths from malaria occurring on the ninth day. There has been an overall mortality rate of 39 per cent within the first forty-eight hours after inoculation, apparently due to the difficulties inherent in the method. Enough embryos survive this early critical period to make the method a practical and reliable one for carrying this parasite in the chick embryo. The presence of a green color in infected embryonic membranes or fluids and in the liver and spleen of the embryo itself permits a ready and easy diagnosis of the presence of malarial infection and obviates the necessity for examining numerous blood films for parasites.

Growth of Pasteurella Tularensis.—Larson shows that Pasteurella tularensis grows readily on chick embryos when introduced into the yolk sac. Chick embryos are as susceptible as mice, and the concentration of organisms in the tissues and fluids of infected chick embryos approaches that obtained in infected mice.

Tennessee State Medical Assn. Journal, Nashville

38:121-152 (May) 1945

Medical Practice in Tennessee. K. C. Copenhaver.—p. 121.
Some Remarks on Osteomalacia in China. F. E. Whitacre.—p. 126.

38:153-202 (June) 1945

Proceedings of the House of Delegates, 112th Annual Meeting, Tennessee State Medical Association, Maxwell House, Nashville, Tennessee April 8, 1945.—p. 153.

United States Naval Med. Bulletin, Washington, D. C.

44:1125-1352 (June) 1945

Foreword to Symposium on Amputation: From the Naval Amputation Center, U. S. Naval Hospital, Mare Island, California. J. P. Owen.—p. 1125.
A. Early Care of Amputation Patients. J. M. Greer.—p. 1128.
B. Definitive Surgical Management of Amputations. H. H. Kessler.—p. 1133.
C. Manufacture and Fitting of Artificial Limbs. D. D. Toffelmier and M. Laurence.—p. 1149.
D. Plastic Surgery of Amputation Stumps. G. B. O'Connor and H. H. Kessler.—p. 1167.
E. Revision of Thigh Amputation. P. F. Olson.—p. 1180.
F. Revision of Below Knee Amputation Stumps. O. S. Nesting.—p. 1187.
G. Painful Stumps and Their Treatment. D. F. Coburn.—p. 1194.
Compression Dressing of Amputation Stumps. D. C. McKeever.—p. 1211.
Transportation of Patients by Naval Air Transport Service. J. P. Pollard, N. L. Yood and J. G. McWilliams.—p. 1213.
Intertrochanteric Fractures of Femur: Early Care on Hospital Ship. H. Lusskin.—p. 1221.
Atmospheric Blast Concussion: Medical Aspects. R. A. Klemm.—p. 1228.
Wounds of Eye, Ear, Nose and Throat. F. P. Smart.—p. 1231.
Thoracic Casualties From the Marianas. H. D. Adams.—p. 1234.
Care of Burn Casualty. F. H. Wanamaker.—p. 1239.
Pneumonia in U. S. Navy—1882-1942: Part II. As Cause of Incapacitation and Mortality. D. F. Smiley and H. A. Raskin.—p. 1245.
*Tropical Eosinophilia: Report of Case. W. R. Hirst and W. J. McCann.—p. 1277.

Tropical Eosinophilia.—Tropical eosinophilia was first described by Weingarten as a disease apparently peculiar to the coastal areas of India. The syndrome is characterized by a gradual onset with malaise, weight loss, a low grade temperature, a paroxysmal dry hacking cough and physical findings similar to those of bronchial asthma. After several weeks a chronic stage is reached, at which time the patient may be subfebrile and the weight loss may cease, but paroxysms of coughing and wheezing may persist. The spleen may be palpable early in the febrile stage. X-ray examination of the chest in the febrile stage reveals a diffuse bilateral mottling of the lung fields, resembling the picture of acute miliary tuberculosis. Subsequent x-ray studies of the lungs reveal increased bronchial markings as in chronic bronchitis. There is massive eosinophilia. Hirst and McCann cite the history of a naval officer who had been on overseas duty in Central America and the Central and South Pacific islands exclusively. The patient had had symptoms of the disease for nearly two years. The dramatic response of the patient to arsenotherapy suggests a spirochetal or protozoan causation. The fact that the patient had never been in India suggests that either the disease exists endemically in the South Pacific area as well as in India or that it is transmissible directly from man to man. This syndrome should be considered in the differential diagnosis of any illness presenting a high eosinophilia. In cases with a massive eosinophilia, when no known cause can be found, a therapeutic trial of an arsenical may be warranted.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Medical Journal of Australia, Sydney

1:313-336 (March 31) 1945

Rubella During Pregnancy of Mother, with Its Sequela of Congenital Defects in Child. N. McA. Gregg.—p. 313.

*Congenital Deaf-Mutism as Sequela of Rubella-like Maternal Infection During Pregnancy. D. G. Carruthers.—p. 315.

Influence of Malaria on Kline and Complement Fixation (Wassermann) Tests for Syphilis. C. B. Cox and M. J. Durant.—p. 320.

Congenital Deaf-Mutism.—Details observed in the study of deaf-mute children whose mothers were infected with rubella during pregnancy are presented. As the result of an appeal to doctors by the New South Wales Department of Public Health, 147 cases of congenital defects have been reported; in 102 of this series a history of maternal rubella was recorded. Of the children 74 are deaf. It has not been possible for Carruthers to tabulate the details of the whole series, but 17 patients have been under his private care. Analyses have been made to determine whether the stage of pregnancy at the time of infection of the mother or the intensity and duration of the mother's illness bears any relation to the nature and degree of congenital abnormalities subsequently to be found in the child. It seems likely that the importance of the stage of pregnancy at which infection occurs is that, if it is in the first six weeks, fetal damage will be widespread and may include the eyes, both divisions of the ears, the heart and perhaps many other parts. After the sixth week the eyes may escape, the heart may be spared and the semicircular canals may become normally developed; but the cochlea is still liable to be damaged, and the growth may be retarded. After the third month damage to the fetus is rare. Many of the children give some evidence of hearing over the tone range 512 to 2,048. In testing the caloric labyrinth reactions there was noted among others that none of the "rubella" group were made sick even when pronounced nystagmus was induced. The utricle and the semicircular canals do not appear to be left untouched by the maternal infection. Regarding associated defects, not 1 of the 17 patients has evidence of cataract. No evidence of ductus arteriosus was observed, but stunting of growth is evident in 11 of 17 patients and microcephaly in 3.

Quarterly Journal of Medicine, Oxford

14:1-56 (Jan.) 1945

Poliomyelitis Epidemic in Malta, 1942-1943. H. J. Seddon, T. Agius, H. G. G. Bernstein and R. E. Tunbridge.—p. 1.

Genetic Linkage in Man, with Particular Reference to Usefulness of Very Small Bodies of Data. J. A. F. Roberts.—p. 27.

*Treatment of Postarsphenamine Jaundice with Sulfur-Containing Amino Acids. R. A. Peters, R. H. S. Thompson and A. J. King, D. I. Williams and C. S. Nicol.—p. 35.

Treatment of Postarsphenamine Jaundice.—Peters and his associates say that, although infection has long been regarded as a probable factor in the etiology of many cases of postarsphenamine jaundice, the arsenicals themselves have never been exonerated. It has been shown repeatedly that the administration of different arsenical compounds to experimental animals can produce damage and necrosis of the liver cells in the absence of coincident spirochetal or other infection. Since a high protein diet can prevent bilirubinemia and liver damage in dogs after weekly intravenous injection of oxophenarsine hydrochloride, it was decided to study the effect of the oral administration of certain sulfur-containing amino acids on the course of postarsphenamine jaundice. The authors studied 468 cases of postarsphenamine jaundice. The conclusions are based on the treatment of 150 severe cases selected from the total of 468. Three groups of patients were treated respectively with cysteine, methionine and casein, control patients being observed simultaneously throughout. The rate of recovery of the patients was observed clinically and by serial estimation of the serum bilirubin levels. A slight but statistically significant increase in the rate of return to normal was noted in the patients receiving cysteine or methionine. Casein, in the dosage used, did not bring about any beneficial effect.

Semana Médica, Buenos Aires

52:469-502 (March 15) 1945. **Partial Index**

*What One Can Expect of Surgical Therapy of Essential Arterial Hypertension. C. Patiño Mayer, L. Lepera, F. A. Pataro and V. F. Pataro.—p. 469.

Sympathectomy in Essential Arterial Hypertension.—Patiño Mayer and his collaborators report good results from sympathectomy followed by potassium thiocyanate therapy early in the phase of malignant essential hypertension and of sympathectomy in essential hypertension with moderate sclerosis with or without spasticity. Blood pressure in his cases returned to normal and remained normal up to date, two or three years after the operation. Symptoms of increased intracranial pressure and of cardiac, renal and pulmonary disturbances and nervousness were greatly diminished. The prognosis as far as the comfort and duration of life is concerned was much improved.

Klinicheskaya Meditsina, Moscow

22:1-80 (Nos. 10 & 11) 1944. **Partial Index**

Treatment of Ulcerative Disease. T. M. Rybakov.—p. 3.

*Symptomatology of Prescorbutic States. M. T. Arinkin.—p. 9.

*Dry Serum Therapy in Albumin Deficiency States. A. A. Bagdasarov, M. S. Dulcin, P. M. Alperin, V. V. Vinogradov and F. E. Loginova.—p. 15.

Symptomatology of Prescorbutic States.—According to Arinkin, one of the first objective symptoms in the incipient stage of scurvy is pallor of the skin and of the conjunctiva. The pallor is probably caused by a spasm of the peripheral blood vessels or by alterations in the blood itself. In the more advanced stage there is pain and tenderness about the joints, particularly of the lower extremities, with a still later appearance of periarticular swellings and discoloration due to hemorrhages into the deep tissues. Some patients complain only of bleeding gums. The author studied 14 patients from 14 to 27 years of age with manifestations of the incipient stage of scurvy. Study of the peripheral blood of these patients revealed insignificant alterations on the part of the red cells, such as mild hypochromia and mild erythropenia. The sternal punctate, however, showed an abnormal increase in the number of microblasts and normoblasts. In the author's experience, in all anemic states, with the exception of aplastic anemia, there exists a parallelism between the degree of anemia and the hyperplasia of the erythroblastic tissue of the bone marrow: the more severe the anemia of the peripheral blood, the greater the percental content of nucleated reds in the bone marrow. This hyperplasia of the erythroblastic tissue of the bone marrow in the preanemic state of scurvy is an index of general intoxication of the organism.

Dry Serum Therapy in Albumin Deficiency States.—Bagdasarov and his associates employed transfusions of dissolved dry human serum in the treatment of clinical states characterized by albumin deficiency. The advantage of this method is that the serum can be given in concentrated solutions with albumin content as high as 28 per cent. Such a serum should exert a favorable effect on osmotic pressure, the water exchange and the tendency to edema. Addition of glucose to the solution increases its effectiveness. The authors administered 170 transfusions to 30 patients with manifestation of alimentary disturbances characterized by symptoms of albumin deficiency, increased capillary permeability and manifestations of hypovitaminosis, chiefly of B_2 and B_1. The dry serum was diluted in concentrations amounting to from two to four times the normal relationship and given every three or four days in amounts varying from 50 to 100 cc. The post-transfusion reactions were few and, when present, were mild. The therapeutic effect was both pronounced and persistent. There was an initial increase followed by decrease in diuresis, disappearance of edema, increase in weight, improvement in muscle tone, termination of diarrhea and normalization of the blood picture. Five patients with alimentary edema treated with repeated small transfusions of conserved blood responded well to this treatment, but the therapeutic effect was not as definite as in the cases treated with concentrated serum solution, particularly with regard to normalization of the albumin content of the blood.

Acta Medica Scandinavica, Stockholm

118:1-260 (Sept. 9) 1944. **Partial Index**

*Type of Respiration in Severe Hypoglycemia. K. Lundbaek.—p. 56.
Iron Content of Serum of the Aged, Particularly in Relation to Chronic Leg Ulcers. S. Eckerström.—p. 69.
Copper in Serum. A. L. Nielsen.—p. 84.
*Renal Changes in Fatal Sulfathiazole Damage. H. Bergstrand.—p. 97.
Metabolism of Copper in Man. A. H. van Ravesteyn.—p. 163.
Nitrous Gas Poisoning Among Welders Using Acetylene Flame: Study of 16 Cases, Including Four Deaths. T. Lindquist.—p. 210.

Respiration in Hypoglycemia.—Lundbaek describes a characteristic type of respiration which occurs during severe hypoglycemia and which has been observed in connection with metabolic experiments. This type of breathing is characterized by the occurrence of varying depth of respiration, jerky expirations and postinspiratory and postexpiratory pauses. This type of respiration is due to a general hypo-oxidation of the cerebrum resulting from hypoglycemia. The hypoglycemic type of respiration may become important in the differential diagnosis between diabetic coma and insulin reaction.

Renal Changes in Fatal Sulfathiazole Damage.—Bergstrand describes the pathologic changes in 7 cases in which sulfathiazole damaged the kidneys. At least 5 of these patients died of uremia. The changes were the same in all cases. They were characterized by focal destruction of the uriniferous tubules at the sites at which sulfathiazole crystals had precipitated. Hyaline protein deposits with perifocal round cell infiltration and hemorrhage were observed around the sulfathiazole crystals in the destroyed tubules. These gave the microscopic picture a characteristic appearance. The renal pelvis showed destruction of epithelium, hemorrhages, and inflammatory cell infiltration in the wall and in the fat of the hilus. The author suggests that inflammatory edema of the kidneys and urinary passages, which was produced by precipitated sulfathiazole crystals, was the chief cause of the uremia.

Nordisk Medicin, Stockholm

22:797-824 (April 28) 1944. **Partial Index**

*Paroxysmal Tachycardia in Infants. J. F. Christensen.—p. 797.
Hormone Elimination in Urine in 2 Male Schizophrenia Patients. E. Høyrup.—p. 801.
Cystic Tumors in Lymphatic Vessels in Ligamentum Latum. V. Albeck.—p. 803.

Hygiea

Are Red Blood Corpuscles in Adults Formed from Erythroblasts? Lisa Boström.—p. 805.

Paroxysmal Tachycardia in Infants.—Christensen says that 37 cases of this disorder in infants have been reported; 7 were in the first week of life, 19 in the first month. About 100 cases in childhood have been reported. Two additional cases in infants aged 3 weeks and 6 months respectively are described. The onset is usually characterized by listlessness, restlessness, loss of appetite, vomiting and diarrhea, with a gradually affected general condition. The cardiac rate during attacks is from 250 to 300. There may be symptoms of heart failure, possibly collapse, convulsions and unconsciousness. There was a congenital heart defect in only 3 of the 37 cases, all fatal. When no organic heart changes are found, the disturbance probably depends on failure of the central or autonomous regulation of the heart. In older children the attacks are more often caused by diseases which have led to injury of the myocardium or of cardiac innervation. The prognosis is good in uncomplicated paroxysmal tachycardia. Digitalis, strophanthin and mecholyl are the most effective drugs.

22:825-890 (May 5) 1944. **Partial Index**

Origin and Fate of Bile Pigments in Organism and Pathogenesis of Jaundice: Review. T. K. With.—p. 825.
Intestinal Perforation Due to Rectoscopy. J. P. Strömbeck.—p. 832.

Hospitalstidende

*Parenteral Iron Therapy: Concluding Reports. S. Dahl.—p. 835.
Roentgen Examination for Pulmonary Tuberculosis as Routine Examination in Hospitals. U. Gad.—p. 837.
Relation Between Clinical Symptoms and Results of Gastroscopy in Patients with Achylia: Gastroscopic Studies, VI. T. Christiansen.—p. 838.

Parenteral Iron Therapy.—The indication for this therapy, intravenous as well as intramuscular, is hypochromic anemia when all other treatment has been ineffective. Intragluteal injections of 11.95 mg. of metallic iron every second or third day gave good results in the 8 cases reported, 2 of which were of anemia after infectious disease, 2 of cancer anemia and 2 of simple anemia. The iron concentration in the serum rose slowly. There were no toxic symptoms. In spite of the immediate by-effects of intravenous iron therapy this method may be more agreeable to the patient than the intramuscular, which seems to give more rapid results but has the drawback of often causing protracted pain at the seat of the injection. Because of the toxicity of iron salts, daily doses above not quite 12 mg. of metallic iron should not be given.

Hygiea

*Diagnostic Value of Chlorine Ion Content in Cerebrospinal Fluid and Relation Between Chlorine Ion in Cerebrospinal Fluid and in Blood. F. Karlström.—p. 839.
Thyrotoxicoses. John Hertz.—p. 856.
Allergy, Hypersensitivity to Histamine and Treatment with Histamine in Various Forms of Headache, Especially Migraine. B. Chronholm.—p. 865.

Chlorine Ion in Cerebrospinal Fluid.—Karlström's material comprises 428 cerebrospinal fluids from 355 patients. In acute poliomyelitis, epilepsy and other diseases of the central and peripheral nervous system the chlorine ion and sugar content of the cerebrospinal fluid and the chloride and sugar index in the blood are within normal limits. In tuberculous meningitis and bacterial (not tuberculous) meningitis the chlorine ion and sugar content of the cerebrospinal fluid and the blood chloride and blood sugar index are lower than normal. Extremely low values for the chlorine ion content of the cerebrospinal fluid point either to tuberculous or to bacterial meningitis; a value lower than 526.5 mg. of sodium chloride per hundred cubic centimeters is pathognomonic for tuberculous meningitis.

22:891-926 (May 12) 1944

Hospitalstidende

Treatment of Gonorrhea with Sulfathiazole and Fever Shock. P. V. Marcussen.—p. 891.
Two Instances of Hypercalcemia (Lymphogranulomatosis Benigna-Hyperparathyroidism). T. Espersen.—p. 894.
Hemeralopia in Patient Treated with Thyroid Which Responded to Administration of Liver Preparation. Karen Marie Hansen.—p. 898.

Hygiea

Orthopedic Treatment of Infantile Paralysis. E. Severin.—p. 899.
Protein Metabolism in Nerve Cells in Connection with Function. H. Hydén.—p. 904.
Experimental Investigation on Physiodynamics of Bullet with Half Casing. H. Hinricsson.—p. 908.

22:927-960 (May 19) 1944. **Partial Index**

Serum Iron in Erythremia (Polycythemia Vera). S. Dahl.—p. 927.
Death After Hysterosalpingography. A. Lachmann.—p. 929.

Finska läk.-sällsk. handl.

Plastic Surgery in War Lesions. P. E. Aschan.—p. 933.

Hygiea

New Strain of Tubercle Bacilli Isolated in England from Voles and Immunization Experiments with It. F. Wahlgren, G. Olin and G. Widström.—p. 943.
Pathologic Heart Condition (Auricular Flutter) in Myotonia. G. Biöck.—p. 946.

22:961-1002 (May 26) 1944

Peridural Anesthesia. N. Blixenkrone-Møller and K. Trautner.—p. 961.

Hygiea

Relation Between Peptic Ulcer and Pulmonary Tuberculosis. E. Forsgren.—p. 973.
*Renal Changes in Myeloma and Their Pathogenesis. R. Lagercrantz.—p. 977.
Compensated Elimination of Ammonia in Renal Insufficiency. J. Tomenius.—p. 981.

Renal Changes in Myeloma.—Study of the unusually large material of 22 cases of myeloma, Lagercrantz says, shows that there is probably a connection between Bence Jones albuminuria and the renal changes in myeloma. The constant changes in myeloma are injury to the tubular epithelium, but the characteristic feature of the disease is the abundant, probably secondary formation of large compact albumin cylinders which block the tubuli, cause inactivity atrophy of the nephrones and stimulate formation of giant cells. In the later stages of the disease a contracted kidney develops.

Book Notices

Penicillin and Other Antibiotic Agents. By Wallace E. Herrell, M.D., M.S., F.A.C.P., Assistant Professor of Medicine, the Mayo Foundation, Rochester, Minn. Cloth. Price, $5. Pp. 348, with 45 illustrations. Philadelphia & London: W. B. Saunders Company, 1945.

A noteworthy accomplishment of the war effort in relation to medicine has been the development of antibiotic therapy. This applies especially to penicillin. Although the advances have been phenomenal, adequate information concerning the therapeutic indications of penicillin has been made available to the medical profession, as well as other pertinent knowledge. Nevertheless in such a rapidly developing field a crystallization of the subject in the form of a monograph is desirable, with the realization, however, that such an effort may be superseded in the near future by information not available at present.

Herrell has endeavored to summarize the extensive fundamental and clinical studies on penicillin and other antibiotic agents. The first hundred pages are devoted to the basic investigations on penicillin. This includes a historical survey; methods of preparation; its physical, chemical and antibacterial properties; absorption, diffusion and excretion, and assay methods. Precise information concerning the chemistry of penicillin is not available, and probably the mechanism of its antibacterial activity is not known.

The succeeding 150 pages are devoted to the clinical use of penicillin. In the main there will be general agreement with the recommendations. Herrell is an enthusiastic advocate of the continuous intravenous method for administering penicillin, particularly to patients with severe infections. His objection to the intermittent, intramuscular mode of injection is that it causes local discomfort and that abrupt rises and falls in blood concentration are not desirable in the therapy of severe infections. One need not utilize 2 to 4 cc. of isotonic solution of sodium chloride for an injection of 10,000 to 20,000 units of penicillin. Most preparations of penicillin now available can be readily dissolved in saline solution, so that only 0.5 to 1 cc. is necessary for such doses. The more convenient intramuscular method may be employed successfully for the treatment of even the severest infections, provided adequate amounts of penicillin are used.

The widest application of penicillin has been made in the management of war wounds, both prophylactically and therapeutically. Several excellent reports have recorded the results in detail. This experience will be of considerable aid in civilian practice. It is unfortunate that more emphasis along these lines has not been incorporated within this monograph. The last section is devoted to other antibiotic agents such as tyrothricin, streptothricin, streptomycin and the less important preparations. The discussion on tyrothricin is one of the best reviews that has appeared. Although interest at present is focused on streptomycin, only twelve lines are devoted to clinical results and no final conclusions are made.

The text is presented in a concise and lucid manner. Each of the twenty-five chapters concludes with key references to the literature. Considering the wartime restrictions, the format, type, grade of paper and the reproduction of illustrations are excellent.

G. I. Nightingale: The Story of an American Army Nurse. By Theresa Archard, Captain, A. N. C. Cloth. Price, $2.50. Pp. 187. New York: W. W. Norton & Company, Inc., 1945.

Captain Archard's story is a story of a typical American girl and her companions, all army nurses. She takes us with her from an American home through a year's "training for defense," through the shock of Pearl Harbor. With her we embark for "overseas." We experience the tedium of waiting, the excitement of unknown perils which lie ahead. We "shake down" our organization—we embark for unknown destinations and finally wade ashore in an amphibious landing. With her we experience the fear, the thrill, the excitement of battle and exult in the justified pride of our task well done. With her and her unit we advance and retreat and advance with the tide of battle. We experience the thrill of a life saved by skill, of comfort and surcease from pain through the work of our hands. In her story we see what a well organized team of doctors, nurses and enlisted men can do for the relief of suffering and the prevention of death, even under the most trying circumstances. In her story we have the record of the 48th Surgical Hospital, which did so much with so little and finally spent itself in its work for its patients, but in so doing pointed the way for the many others which followed it.

The story is authentic. Captain Archard has captured the moods of the men and women who make medical history in the armed forces. She calls her story "G. I. Nightingale." "G. I." is commonly interpreted as "Government Issue"; it might well be paraphrased "Granite, Iron," for the women of this historical record are made of rigid stuff. Florence Nightingale would be truly proud of her successors.

How parallel is this record with that of Florence Nightingale in the Crimea! As Florence Nightingale brought cleanliness to Scutari and reduced its death rate from 47 per cent to 2 per cent, so do our nurses bring cleanliness to our improvised military hospitals around the world and in so doing make it possible for those who have fallen in battle to rise up and walk the earth again.

This story illustrates woman's great contribution to modern medicine. It shows at its best that unbeatable team the Doctor and the Nurse.

It is a story of hard work, of winning against great odds; but through it all Captain Archard never loses her sense of humor. She laughs at her fears, she laughs at her plights, she laughs at herself and her nurses in soldier's coveralls. She laughs at her skinny body wasted from short rations and North African malaria.

Técnica e tática na calculose do hépatocolédoco. Por Piragibe Nogueira, Docente livre de Clinica cirurgica da Faculdade de medicina da Universidade de São Paulo. Paper. Pp. 117, with illustrations. São Paulo, 1944.

In this work, which is Dr. Piragibe's thesis presented to the Faculty of Medicine of São Paulo in partial fulfilment of the right to conduct courses in operative surgery at the medical school, the author summarizes his experience in dealing with hepaticocholedochal lithiasis, besides discussing the literature. It is a concise synopsis on the subject, with 140 references.

The monograph is divided into eight chapters, on history, definition, anesthesia, surgical anatomy of the biliary ducts, access to the biliary ducts, exploration and operative technic, secondary operations and case reports, conclusions and references. In the chapter on surgical anatomy the author describes the various pitfalls that exist in operating on the gallbladder, illustrating the different anomalies that can be found in the ducts, their blood supply and their relation to the hepatic blood vessels. Dissection on cadavers substantiates the author's statements. Although no personal statistical data are given and only case reports are published, the author shows experience in this field; he is of the opinion that operative cholangiography is of value but not an essential means of exploration in the hands of an experienced surgeon who can make good use of palpation, probing and irrigation for assuring patency of bile ducts.

A Study of Certified Sickness Absence Among Women in Industry. By S. Wyatt, assisted by R. Marriott, W. M. Dawson, Norah M. Davis, D. E. R. Hughes and F. G. L. Stock. Medical Research Council, Industrial Health Research Board, Report No. 86. Paper. Price, 9d. Pp. 34, with 4 illustrations. London: His Majesty's Stationery Office, 1945.

This investigation substantiates in large measure American experience in the employment of women. Twenty thousand women were observed. Respiratory, digestive and functional nervous disorders were most serious offenders. Gynecologic disorders are relatively unimportant as reflected in average days of sickness per worker, but in average length of individual absence they rank first in the married group and second in the single. Seven and eight tenths per cent of the total work days were lost. Married women lost 17.4 days, single women 10.6. Conditions of work had recognizable effect on sick absence. The importance of good medical and attendance records in industry is stressed. Although these studies were carefully controlled and based on certified absences of two days or more, there are many factors which affect lost time not directly assignable to health but which nevertheless are reflected in the statistics.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SIGNIFICANCE OF LOW BASAL METABOLIC RATE —THYROID EXTRACT AND VITAMIN B.

To the Editor:—Does taking thyroid, either the right amount or an overdosage, take up the vitamin B from the system? What conditions other than hypothyroidism would account for a low basal metabolic rate?

George A. Bakke, M.D., Oakland, Calif.

ANSWER.—The administration of desiccated thyroid and the presence of hyperthyroidism appear to increase the requirement of the body for vitamin B. However, if the diet is well balanced and adequate in amount supplementary therapy with B complex is not necessary. It has been suggested that the administration of vitamin B_1 to patients with hyperthyroidism is valuable in improving their preoperative condition. The evidence for this statement is not convincing.

There is a large group of patients with basal metabolic rates of —15 to —25 per cent who do not appear to have hypothyroidism. When their rates are increased by the administration of desiccated thyroid these patients become nervous and suffer from palpitation, indicating that the slight depression in their level of metabolism may not be the result of hypothyroidism. An important cause of low basal metabolism is, of course, hypopituitarism, but in this condition the low metabolism is a result of hypothyroidism which develops secondary to the pituitary deficiency. In patients with this abnormality, raising the metabolism by the administration of thyroid produces definite improvement but does not correct many of the abnormalities that are not related to the hypothyroidism, as, for example, the hypogonadism.

In patients with myxedema the basal metabolism may be raised to normal with dinitrophenol without producing any effect on the myxedematous condition. Observations such as these indicate that there may be many factors controlling the total metabolism that are not clearly understood at present. When one is faced with the problem of determining whether or not hypothyroidism is present, the best thing is probably to make a therapeutic trial of administering thyroid. If improvement occurs when enough is given to raise the basal metabolism to normal it may be concluded that hypothyroidism is the cause of the low rate. If improvement does not result, it may be concluded that hypothyroidism is not present and the administration of thyroid may actually be harmful.

TOXICITY OF PARALDEHYDE AND INSOMNIA

To the Editor:—What is the effect of prolonged daily administration of paraldehyde in doses of 8 to 16 cc.? Is this likely to produce toxic symptoms or harmful effects? I have a patient who suffers from insomnia and this is the only thing that produces sleep now. She has taken barbital and its derivatives in doses of 10 to 20 grains almost daily for the past ten to fifteen years, and it no longer produces the desired result. She has been treated by prominent psychiatrists without definite effect. At that time she was getting results with barbital, and they told her she would have to continue it the rest of her life. I know that continued use of paraldehyde is likely to produce chronic poisoning with symptoms similar to chronic alcoholism, but what about the toxicity in regard to internal organs? Has paraldehyde been administered over indefinite periods without harmful effects? Can any other drug be suggested for this patient? Chloral hydrate has been tried. What will disguise the odor of paraldehyde on the breath? M.D., South Carolina.

ANSWER.—The chronic toxicity of paraldehyde is not well known but is generally stated to be similar to that of alcohol, including the mental aberrations. Tolerance may develop. A postmortem examination of a man who had taken 4 to 8 cc. of paraldehyde daily for several months, and 75 cc. or more on his final night, showed principally hyperemia of the stomach and upper intestine, without any severe visceral degenerations (McFall, J. E. W.: Paraldehyde Poisoning, *Brit. M. J.* **2**:255 [Aug. 8] 1925). There is no way to disguise the odor of paraldehyde on the breath. Nightly sedation for insomnia is unwise. Daytime problems carried over into the night, or a simple habit of inversion of sleep, may be responsible and should be approached from the psychotherapeutic standpoint, if possible. Rather than substitute another drug for a person who is obviously easily habituated, a period of institutional care under a psychiatrist is suggested.

COUGH REMEDIES

To the Editor:—I have been accustomed to prescribe guaiacol carbonate or terpin hydrate for coughs that were or showed a tendency to become chronic. Now these two drugs are discontinued because they were deleted from the U. S. Pharmacopeia. What is recommended in their place?

M.D., New York.

ANSWER.—So far as is known guaiacol carbonate and terpin hydrate are still official in the National Formulary and the U. S. Pharmacopeia. Guaiacol carbonate is highly insoluble and probably inactive with respect to cough. Terpin hydrate, although of long empiric usage, also is of questionable value either to reduce or to lessen cough.

When coughing is unproductive and associated with a "tickle" in the throat, any substance with a strong local action is likely to bring relief. Sweet, alcoholic preparations with a pungent taste are effective. One such agent is Elixir of Terpin Hydrate, N. F., to which the terpin hydrate presumably lends only flavor. Others are Aromatic Elixir, U. S. P., and Elixir of Glycyrrhiza, U. S. P.

When the cough is persistent, and especially if it is productive, suppression is indicated but should be intermittent, to allow drainage of the bronchial tree on the one hand and yet prevent the fatigue of constant coughing. For this purpose codeine is the agent of choice in doses of 15 mg. administered every three or four hours. It is preferably dispensed in liquid form, to obscure the bitter taste, and to add to the local effect in the mouth and throat. For this purpose any of the vehicles previously mentioned may be used.

Like terpin hydrate, sodium iodide and ammonium chloride are drugs of long usage in cough, particularly with the intent of thinning tenacious sputum. Here also the alleged effect appears to be greatly exaggerated over that actually produced.

POSITIVE WASSERMANN REACTION AND BOECK'S SARCOID

To the Editor:—What is the significance of a 4 plus Wassermann reaction in the presence of Boeck's sarcoid? What is now considered to be the best form of treatment? What is the prognosis? M.D., Oklahoma.

ANSWER.—Boeck's sarcoid is regarded by some investigators as an atypical form of tuberculosis, although others disagree with this view. Placing it in the group of inflammatory diseases, one must consider the possibility of a false positive serologic reaction for syphilis. B. D. Davis (Biologic False Positive Serologic Tests for Syphilis, *Medicine* **23**:359 [Dec.] 1944) has studied this problem very thoroughly. Among the diseases listed in which such a false positive test may occur are tuberculosis and miscellaneous infections. Davis also outlines the requirements for a verification test. Therefore, control studies (Kahn test, quantitative Wassermann test) are indicated in a case of Boeck's sarcoid with a 4 plus Wassermann reaction before definitely establishing the clinical diagnosis of syphilis. In this connection it is interesting to note that quite frequently hyperglobulinemia is found in patients with Boeck's sarcoid. However, as Davis points out, "there appears to be a widespread but unwarranted impression that false positive serologic tests are often caused by any conditions which give rise to a marked hyperglobulinemia."

Treatment of Boeck's sarcoid has usually been purely empirical and includes the use of arsenicals, tuberculin, iodides, gold salts, hyperpyrexia, ultraviolet irradiation, roentgen rays and radium. The latter have been successful in the treatment of skin lesions, particularly in the Darier-Roussy type, and also in the Boeck lesion. Evaluation of any form of treatment is difficult because of the tendency of the lesions to spontaneous resolution. Earlier workers have not found roentgen therapy of benefit in the systemic lesions. Middleton sums up this experience in the latest edition of Cecil's Textbook of Medicine with the statement that roentgen and radium therapy offer nothing in this disease. Recently, however, several reports on the treatment of enlarged lymph nodes and of hilar and pulmonary sarcoid have been favorable. Pohle and his associates (Pohle, E. A.; Paul, L. W., and Clark, Elizabeth A.: Roentgen Therapy of Boeck's Sarcoid, *Am. J. M. Sc.* **209**:503 [April] 1945) recommend moderate doses of roentgen rays applied either to the mediastinum or to the involved lymph glands, using the same technic as is customary in the treatment of inflammatory disease. Eight of their 14 cases were observed sufficiently long to permit at least preliminary conclusions: in 4 of the first 8 cases the therapeutic result was good, in 1 instance excellent, in 1 satisfactory and in 2 only fair. Untoward reactions were not observed in any one of their treated cases.